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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page for STN Seminar Schedule - N. America
 NEWS  2  JUN 06   EPFULL enhanced with 260,000 English abstracts
 NEWS  3  JUN 06   KOREAPAT updated with 41,000 documents
 NEWS  4  JUN 13   USPATFULL and USPAT2 updated with 11-character
                   patent numbers for U.S. applications
 NEWS  5  JUN 19   CAS REGISTRY includes selected substances from
                   web-based collections
 NEWS  6  JUN 25   CA/CAplus and USPAT databases updated with IPC
                   reclassification data
 NEWS  7  JUN 30   AEROSPACE enhanced with more than 1 million U.S.
                   patent records
 NEWS  8  JUN 30   EMBASE, EMBAL, and LEMBASE updated with additional
                   options to display authors and affiliated
                   organizations
 NEWS  9  JUN 30   STN on the Web enhanced with new STN AnaVist
                   Assistant and BLAST plug-in
 NEWS 10  JUN 30   STN AnaVist enhanced with database content from EPFULL
 NEWS 11  JUL 28   CA/CAplus patent coverage enhanced
 NEWS 12  JUL 28   EPFULL enhanced with additional legal status
                   information from the epoline Register
 NEWS 13  JUL 28   IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
 NEWS 14  JUL 28   STN Viewer performance improved
 NEWS 15  AUG 01   INPADOCDB and INPAFAMDB coverage enhanced
 NEWS 16  AUG 13   CA/CAplus enhanced with printed Chemical Abstracts
                   page images from 1967-1998
 NEWS 17  AUG 15   CAOLD to be discontinued on December 31, 2008
 NEWS 18  AUG 15   CAplus currency for Korean patents enhanced
 NEWS 19  AUG 27   CAS definition of basic patents expanded to ensure
                   comprehensive access to substance and sequence
                   information
 NEWS 20  SEP 18   Support for STN Express, Versions 6.01 and earlier,
                   to be discontinued
 NEWS 21  SEP 25   CA/CAplus current-awareness alert options enhanced
                   to accommodate supplemental CAS indexing of
                   exemplified prophetic substances
 NEWS 22  SEP 26   WPIDS, WPINDEX, and WPIX coverage of Chinese and
                   and Korean patents enhanced
 NEWS 23  SEP 29   IFICLS enhanced with new super search field
 NEWS 24  SEP 29   EMBASE and EMBAL enhanced with new search and
                   display fields
 NEWS 25  SEP 30   CAS patent coverage enhanced to include exemplified
                   prophetic substances identified in new Japanese-
                   language patents
 NEWS 26  OCT 07   EPFULL enhanced with full implementation of EPC2000
 NEWS 27  OCT 07   Multiple databases enhanced for more flexible patent
                   number searching
 NEWS 28  OCT 22   Current-awareness alert (SDI) setup and editing
                   enhanced
 NEWS 29  OCT 22   WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT
                   Applications

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 12:35:50 ON 22 OCT 2008

=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 12:35:58 ON 22 OCT 2008

 FILE LAST UPDATED: 21 Oct 2008 (20081021/UP).  FILE COVERS 1949 TO DATE.

  MEDLINE has been updated with the National Library of Medicine's
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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

  See HELP RANGE before carrying out any RANGE search.

  MEDLINE Accession Numbers (ANs) for records from 1950-1977 have
  been converted from 8 to 10 digits.  Searches using an 8 or 10 digit
  AN will retrieve the same record.  The 10-digit ANs can be expanded,
  searched, and displayed in all records from 1949 to the present.

=> s genotyp? and risk and (cardiovascular or (cardio and vascular) or CVD)
        142266 GENOTYP?
        949673 RISK
         86065 RISKS
        983213 RISK
                  (RISK OR RISKS)
        236681 CARDIOVASCULAR
             6 CARDIOVASCULARS
        236684 CARDIOVASCULAR
                  (CARDIOVASCULAR OR CARDIOVASCULARS)
          7944 CARDIO
        424724 VASCULAR
             4 VASCULARS
        424726 VASCULAR
                  (VASCULAR OR VASCULARS)
          6937 CVD
           159 CVDS
          6989 CVD
                  (CVD OR CVDS)
L1        2144 GENOTYP? AND RISK AND (CARDIOVASCULAR OR (CARDIO AND VASCULAR)
               OR CVD)

=> s l1 and relative risk
        394433 RELATIVE
         28704 RELATIVES
        420024 RELATIVE
                  (RELATIVE OR RELATIVES)
        949673 RISK
         86065 RISKS
        983213 RISK
                  (RISK OR RISKS)
         37111 RELATIVE RISK
                  (RELATIVE(W)RISK)
L2          80 L1 AND RELATIVE RISK

=> d bib ab 1-80

L2   ANSWER 1 OF 80     MEDLINE on STN
Full Text
AN   2008511270     MEDLINE
DN   PubMed ID: 18672474
TI   Interrelationships among the MTHFR 677C>T polymorphism, migraine, and
     cardiovascular disease.
```

AU Schurks Markus; Zee Robert Y L; Buring Julie E; Kurth Tobias
CS Department of Medicine, Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA 02215-1204, USA.
NC CA-47988 (United States NCI)
HL-080467 (United States NHLBI)
HL-43851 (United States NHLBI)
SO Neurology, (2008 Aug 12) Vol. 71, No. 7, pp. 505-13. Electronic Publication: 2008-07-30.
Journal code: 0401060. E-ISSN: 1526-632X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200810
ED Entered STN: 13 Aug 2008
Last Updated on STN: 15 Oct 2008
Entered Medline: 14 Oct 2008
AB BACKGROUND: Interrelationships among the MTHFR 677C>T polymorphism (rs1801133), migraine, and **cardiovascular** disease (**CVD**) are plausible but remain controversial. METHODS: Association study among 25,001 white US women, participating in the Women's Health Study, with information on MTHFR 677C>T polymorphism. Migraine and migraine aura status were self-reported. Incident **CVD** events were confirmed after medical record review. We used logistic regression to investigate the **genotype**-migraine association and proportional hazards models to evaluate the interrelationships of **genotype** and migraine on incident **CVD**. RESULTS: At baseline, 4,577 (18.3%) women reported history of migraine; 39.5% of the 3,226 women with active migraine indicated aura. During a mean of 11.9 years of follow-up, 625 **CVD** events occurred. Carriers of the TT **genotype** were less likely to have migraine with aura. The multivariable-adjusted **relative risk** (RR) in the recessive model was 0.79 (95% CI = 0.65-0.96; p = 0.02). The TT **genotype** did not increase the **risk** for **CVD**. In contrast, migraine with aura doubled the **risk** for **CVD** (multivariable-adjusted RR = 2.06; 95% CI = 1.53-2.78; p < 0.0001). Coexistence of migraine with aura and the TT **genotype** selectively raised this **risk** (RR = 3.66; 95% CI = 1.69-7.90; p = 0.001). This pattern was driven by a fourfold increased **risk** for ischemic stroke (multivariable-adjusted RR = 4.19; 95% CI = 1.38-12.74; p = 0.01) and was not apparent for myocardial infarction. CONCLUSIONS: Data from this large cohort of women suggest a modest protective effect of the MTHFR 677TT **genotype** on migraine with aura. The increased **risk** for **cardiovascular** disease among migraineurs with aura was magnified for TT **genotype** carriers, which was driven by a substantially increased **risk** of ischemic stroke.

L2 ANSWER 2 OF 80 MEDLINE on STN
Full Text
AN 2007673974 MEDLINE
DN PubMed ID: 17290100
TI Serum chitotriosidase activity, a marker of activated macrophages, predicts new **cardiovascular** events independently of C-reactive protein.
AU Artieda Marta; Cenarro Ana; Ganan Alberto; Lukic Antonela; Moreno Eva; Puzo Jose; Pocovi Miguel; Civeira Fernando
CS Laboratorio de Investigacion Molecular, Hospital Universitario Miguel Servet, Zaragoza, Spain.. martieda@salud.aragon.es
SO Cardiology, (2007) Vol. 108, No. 4, pp. 297-306. Electronic Publication: 2007-02-09.
Journal code: 1266406. E-ISSN: 1421-9751.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200801
ED Entered STN: 20 Nov 2007
Last Updated on STN: 12 Jan 2008
Entered Medline: 10 Jan 2008
AB BACKGROUND: C-reactive protein (CRP) is a well-established inflammation marker associated with **cardiovascular risk**. However, its relationship with chitotriosidase activity, a novel marker of activated macrophages

highly expressed in human atherosclerotic plaques, is unknown. Therefore, we sought to determine if serum chitotriosidase activity predicts the **risk** of new coronary events, and to analyze its relationship with CRP. METHODS: Chitotriosidase activity and **genotype**, and high-sensitivity CRP were measured at baseline in 133 middle-aged men with stable coronary heart disease, who were followed for the occurrence of **cardiovascular** morbidity and mortality for a mean of 4 years. We studied the value of these proteins in predicting the **risk** of new **cardiovascular** events. RESULTS: Serum chitotriosidase activity was higher in the group of subjects with a prespecified major event (nonfatal myocardial infarction, nonfatal ischemic stroke, coronary revascularization procedures and death from **cardiovascular** causes) than in the group of subjects without event, 116 +/- 30.9 nmol/ml x h versus 74.2 +/- 5.69 nmol/ml x h, respectively (p = 0.042). The baseline values of chitotriosidase activity and CRP did not correlate (R = 0.104, p = 0.266), but both parameters were related to a reduction of event-free survival in the Cox regression analysis, with **relative risks** of 2.61 (p = 0.060) and 2.56 (p = 0.019), respectively. Chitotriosidase activity seems to be a better marker for new events occurring after 2 years of follow-up than in the first 2 years. Both markers had similar predictive values, and their sensitivity (64%) and negative predictive value (84%) were improved when combined. CONCLUSIONS: Our results suggest that serum chitotriosidase activity predicts the **risk** of new **cardiovascular** events in the following 4 years. This new **cardiovascular risk** marker is independent of CRP and, when combined, the prediction of the **risk** of new **cardiovascular** events and the identification of a lower **risk** group seem to improve.

L2 ANSWER 3 OF 80 MEDLINE on STN
Full Text
AN 2007599381 MEDLINE
DN PubMed ID: 17919541
TI Efficacy and safety of inhaled zanamivir in the prevention of influenza in community-dwelling, high-**risk** adult and adolescent subjects: a 28-day, multicenter, randomized, double-blind, placebo-controlled trial.
AU LaForce Craig; Man Choy Y; Henderson Frederick W; McElhaney Janet E; Hampel Frank C Jr; Bettis Robert; Kudule Laila; Harris Julia; Yates Philip; Tisdale Margaret; Webster Alison
CS North Carolina Clinical Research Inc., Raleigh, North Carolina, USA.
SO Clinical therapeutics, (2007 Aug) Vol. 29, No. 8, pp. 1579-90; discussion 1577-8.
Journal code: 7706726. ISSN: 0149-2918.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(CLINICAL TRIAL)
LA English
FS Priority Journals
EM 200712
ED Entered STN: 10 Oct 2007
Last Updated on STN: 11 Dec 2007
Entered Medline: 6 Dec 2007
AB BACKGROUND: Influenza can cause significant morbidity and mortality in subjects at high **risk** for complications, including the elderly (age >or=65 years) and those with chronic respiratory, **cardiovascular**, or metabolic conditions. Effective prophylaxis can significantly reduce the disease burden in this population. Previous studies conducted primarily in non-high-**risk** subjects have reported the efficacy of inhaled zanamivir in preventing influenza. OBJECTIVE: This study investigated the efficacy and safety of zanamivir in preventing influenza in community-dwelling adult and adolescent subjects at high **risk** for complications of influenza. METHODS: This was a multicenter, randomized, double-blind, placebo-controlled, parallel-group study in community-dwelling subjects aged >or=12 years who were at high **risk** for developing complications of influenza, were able to use the Diskhaler device (Glaxo Group Limited, Research Triangle Park, North Carolina), and were able to take the first dose of study medication within 5 days of laboratory-confirmed local influenza activity. Eligible subjects were randomized to receive inhaled zanamivir 10 mg or placebo once daily for 28 days. The primary end point was the proportion of randomized subjects who

developed symptomatic influenza during prophylaxis, as confirmed by culture and/or serology. All adverse events (AEs) occurring after the first dose of study medication were recorded. RESULTS: The study enrolled 3363 subjects, of whom 58% were female and 93% were white; the mean age of participants was 60.4 years (range, 12-94 years), and 4% were adolescents. Significantly fewer zanamivir-treated subjects developed symptomatic, laboratory- confirmed influenza during prophylaxis compared with placebo recipients (4/1678 vs 23/1685, respectively), representing a **relative risk** (RR) of 0.17 (95% CI, 0.07-0.44; P < 0.001) and a protective efficacy of 83%. The incidence of complications was reduced in zanamivir-treated subjects compared with placebo recipients (1/1678 and 8/1685), representing an RR of 0.12 (95% CI, 0.02-0.73; P = 0.042) and a protective efficacy of 88%. The numbers of zanamivir recipients (151/1678 [9%]) and placebo recipients (169/1685 [10 %]) who developed symptomatic influenza-like illness regardless of laboratory confirmation did not differ significantly (RR = 0.86; 95% CI, 0.70-1.06), indicating that zanamivir was not effective in preventing influenza-like illness that was not caused by influenza infection. Similarly, there was no significant difference in the numbers of zanamivir and placebo recipients who developed laboratory-confirmed infection regardless of symptoms (39/1678 [2%] and 52/1685 [3%], respectively; RR = 0.76; 95% CI, 0.50-1.15). Of these, 64 subjects (35 and 29) were asymptomatic; seroconversion occurred in all but 1 subject, indicating that zanamivir prophylaxis did not prevent asymptomatic seroconversion. During prophylaxis, 51% of subjects in both treatment groups reported at least 1 AE. There were no major differences in the frequency or nature of AEs between groups. The most commonly reported AEs (>or=3% of subjects in each treatment group) were consistent with upper respiratory viral infection (headache: 17% zanamivir, 18% placebo; cough: 14% and 15%, respectively; throat and tonsil discomfort/pain: 13% and 14%). There were no differences between groups in the overall incidence of viral respiratory infections (5% in both groups) or ear, nose, and throat infections (2% in both groups). None of the analyzed isolates from confirmed cases of influenza exhibited reduced susceptibility to zanamivir or **genotypic** evidence of resistance. CONCLUSIONS: Zanamivir, administered once daily for 28 days, was efficacious in preventing infection with the predominant circulating strains in the 2000- 2001 influenza season in the Northern Hemisphere (influenza A/New Calendonia/20/99-like and influenza B/ Sichuan/379/99-like) in these high-**risk** community- dwelling subjects aged >or=12 years. Zanamivir was well tolerated, with a safety profile comparable to that of placebo. No emergence of resistant virus was detected.

L2 ANSWER 4 OF 80 MEDLINE on STN
Full Text
AN 2007502297 MEDLINE
DN PubMed ID: 17452407
TI Association between oestrogen receptor alpha gene polymorphism and mortality in female end-stage renal disease patients.
AU Kato Sawako; Lindholm Bengt; Axelsson Jonas; Qureshi Rashid A; Barany Peter; Heimburger Olof; Gustafsson Jan-Ake; Stenvinkel Peter; Nordfors Louise
CS Division of Renal Medicine, Department of Clinical Science, Intervention and Technology, Karolinska University Hospital Huddinge, K-56, 141 86, Stockholm, Sweden.
SO Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, (2007 Sep) Vol. 22, No. 9, pp. 2571-7. Electronic Publication: 2007-04-23.
Journal code: 8706402. ISSN: 0931-0509.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200711
ED Entered STN: 29 Aug 2007
Last Updated on STN: 8 Dec 2007
Entered Medline: 30 Nov 2007
AB BACKGROUND: In the general population, genetic variations in the oestrogen receptor alpha (ERalpha) gene may influence lipid abnormalities,

cardiovascular disease (**CVD**), and mortality, but this has not previously been studied in end-stage renal disease (ESRD) patients. METHODS: A total of 227 ESRD (141 men and 86 women) patients starting renal replacement therapy (RRT) were **genotyped** for three ERalpha gene polymorphisms (Ser10Ser, PvuII and XbaI) and the associations between these polymorphisms and clinical and laboratory parameters and survival were analysed. Patients were followed for a median period of 55 months (range 1-126 months). RESULTS: The PvuII and XbaI polymorphisms were not associated with any of the clinical parameters. The ERalpha Ser10Ser CC **genotype** was present in 24 (28%) of the female and in 37 (26%) of the male patients. When comparing the CC **genotype** with the CT and TT **genotypes**, there were significant differences in lipid levels and inflammatory marker levels, especially in female patients. In female patients, the CC **genotype** was associated with lower prevalence of protein energy wasting (PEW) (17.4% vs 43.1%; P=0.03), lower median serum triglyceride (1.7 vs 2.1 mmol/l; P=0.001), higher median serum albumin (34.0 vs 32.5 g/l; P=0.03) and lower median high sensitivity-CRP (hsCRP) (2.2 vs 5.5 mg/l; P=0.03) levels compared with the CT plus TT **genotypes**. In male patients only HDL-cholesterol and ApoA levels were associated with this polymorphism. Whereas this polymorphism did not influence survival in males, the mortality was lower in female patients with the CC **genotype** (Kaplan-Meier; Log-rank 2.2, P=0.02). Moreover, female patients with the CT plus TT **genotypes** had a borderline significant increased **relative risk** (Cox hazard model; 6.6, 95% CI: 0.87-49.9 P=0.06) of death as compared with those with the CC **genotype**, even after adjustment for age and prevalence of **CVD**. CONCLUSIONS: Female, but not male ESRD patients with the ERalpha Ser10Ser CC **genotype** had lower prevalence of PEW, lower serum triglyceride, higher serum albumin and lower hsCRP levels. As this **genotype** was associated with a significantly decreased **risk** of all-cause death during the initial years of RRT, its protective properties need further study.

L2 ANSWER 5 OF 80 MEDLINE on STN
Full Text
AN 2007493117 MEDLINE
DN PubMed ID: 17712123
TI Single nucleotide polymorphisms at the adiponectin locus and **risk** of coronary heart disease in men and women.
AU Pischon Tobias; Pai Jennifer K; Manson JoAnn E; Hu Frank B; Rexrode Kathryn M; Hunter David; Rimm Eric B
CS Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts, USA.. pischon@mail.dife.de
NC CA55075 (United States NCI)
HL34594 (United States NHLBI)
HL35464 (United States NHLBI)
SO Obesity (Silver Spring, Md.), (2007 Aug) Vol. 15, No. 8, pp. 2051-60. Journal code: 101264860. ISSN: 1930-7381.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200711
ED Entered STN: 23 Aug 2007
Last Updated on STN: 4 Nov 2007
Entered Medline: 2 Nov 2007
AB OBJECTIVE: The objective was to examine the association of 5 common single nucleotide polymorphisms (SNPs) at the adiponectin locus with **risk** of coronary heart disease (CHD) in men and women. METHODS AND PROCEDURES: We **genotyped** five common SNPs in the adiponectin gene (rs266729, -11365C>G; rs822395, -4034A>C; rs822396, -3964A>G; rs2241766, +45T>G; and rs1501299, +276G>T) in men (Health Professionals Follow-up Study) and women (Nurses' Health Study) in a nested case control setting. Among participants free of **cardiovascular** disease at baseline, 266 men and 249 women developed non-fatal myocardial infarction or fatal CHD during 6 and 8 years of follow-up, respectively. In addition, 564 men had coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty. Using **risk** set sampling, controls were selected 2:1 matched on age, smoking, and date of blood draw. RESULTS: The -4034CC **genotype** was related to an increased **risk** of non-fatal myocardial infarction or fatal CHD compared with the AA **genotype** [**relative risk** (RR), men, 1.69; 95% confidence

interval (CI), 0.99 to 2.89; women, 2.04; 95% CI, 1.20 to 3.49); however, this **genotype** was not related to **risk** of coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty or to plasma adiponectin levels. Other SNPs or haplotypes defined by the 5 SNPs were not consistently related to **risk** of CHD in men and women or to plasma adiponectin levels. DISCUSSION: Our study does not support the hypothesis that these 5 common SNPs in the adiponectin gene play an important role in the development of CHD among men and women, although we cannot exclude an association between the -4034CC **genotype** and **risk** of CHD.

L2 ANSWER 6 OF 80 MEDLINE on STN
Full Text
AN 2007491720 MEDLINE
DN PubMed ID: 17622934
TI The endothelial nitric oxide synthase gene -786T/C polymorphism is a predictive factor for reattacks of coronary spasm.
AU Nishijima Tsunenori; Nakayama Masafumi; Yoshimura Michihiro; Abe Koji; Yamamuro Megumi; Suzuki Satoru; Shono Makoto; Sugiyama Seigo; Saito Yoshihiko; Miyamoto Yoshihiro; Nakao Kazuwa; Yasue Hirofumi; Ogawa Hisao
CS The Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan.
SO Pharmacogenetics and genomics, (2007 Aug) Vol. 17, No. 8, pp. 581-7.
Journal code: 101231005. ISSN: 1744-6872.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200709
ED Entered STN: 23 Aug 2007
Last Updated on STN: 20 Sep 2007
Entered Medline: 19 Sep 2007
AB OBJECTIVE: We previously found a -786T/C polymorphism in the 5'-flanking region of the endothelial nitric oxide synthase (eNOS) gene and reported that this polymorphism is strongly associated with coronary spasm. In this study, we examined whether the polymorphism is a prognostic marker in coronary spasm patients. METHODS AND RESULTS: We examined the clinical courses of 201 consecutive patients with coronary spasm who were admitted to our institution: 146 patients with the -786T/T **genotype**; 50 patients with the -786C/T **genotype**; and five patients with the -786C/C **genotype**. The mean follow-up period was 76+/-60 months. All the patients took calcium channel blockers and/or nitrate during the follow-up period. In this study, no patients died due to a cardiac event. About 25 patients were readmitted owing to **cardiovascular** disease. Out of these 25 patients, 23 patients were readmitted owing to a reattack of coronary spasm. The -786C allele was significantly associated with readmission due to coronary spasm (P=0.0072, odds ratio: 3.37 in the dominant effect). Kaplan-Meier analysis revealed that the occurrence of readmission was significantly higher in the patients with the -786C allele than in the patients without the -786C allele (P=0.0079). Further, multiple logistic regression analysis revealed that the -786T/C polymorphism was an independent predictor for readmission due to reattack of coronary spasm (P=0.006; **relative risk**=3.590). CONCLUSIONS: The eNOS -786C allele is an independent **risk** factor for readmission due to a recurrent attack of coronary spasm in patients with coronary spasm, even if the patients have taken calcium channel blockers and/or nitrate.

L2 ANSWER 7 OF 80 MEDLINE on STN
Full Text
AN 2007391765 MEDLINE
DN PubMed ID: 17577421
TI The impact of the catechol-O-methyltransferase Val158Met polymorphism on survival in the general population--the HUNT study.
AU Hagen Knut; Stovner Lars J; Skorpen Frank; Pettersen Elin; Zwart John-Anker
CS Department of Clinical Neuroscience, Faculty of medicine, Norwegian University of Science and Technology, Trondheim, Norway.. knut.hagen@ntnu.no
SO BMC medical genetics, (2007) Vol. 8, pp. 34. Electronic Publication: 2007-06-19.
Journal code: 100968552. E-ISSN: 1471-2350.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 200707
ED Entered STN: 6 Jul 2007
Last Updated on STN: 7 Jul 2007
Entered Medline: 6 Jul 2007
AB BACKGROUND: The catechol-O-methyltransferase (COMT) gene contains a functional polymorphism, Val158Met which has been related to common diseases like cancer, psychiatric illness and myocardial infarction. Whether the Val158Met polymorphism is associated with survival has not been evaluated in the general population. The aim of this prospective study was to evaluate the impact of codon 158 COMT gene polymorphism on survival in a population-based cohort. METHODS: The sample comprised 2979 non-diabetic individuals who participated in the Nord-Trondelag Health Study (HUNT) in the period 1995-97. The subjects were followed up with respect to mortality throughout year 2004. RESULTS: 212 men and 183 women died during the follow up. No association between codon 158 COMT gene polymorphism and survival was found. The unadjusted **relative risk** of death by non-ischemic heart diseases with Met/Met or Met/Val **genotypes** was 3.27 (95% confidence interval, 1.19-9.00) compared to Val/Val **genotype**. When we adjusted for age, gender, smoking, coffee intake and body mass index the **relative risk** decreased to 2.89 (95% confidence interval, 1.04-8.00). CONCLUSION: During 10 year of follow-up, the Val158Met polymorphism had no impact on survival in a general population. Difference in mortality rates from non-ischemic heart diseases may be incidental and should be evaluated in other studies.

L2 ANSWER 8 OF 80 MEDLINE on STN
Full Text
AN 2007334808 MEDLINE
DN PubMed ID: 17512633
TI An increased incidence of Enterobacter cloacae in a **cardiovascular** ward.
AU Kanemitsu K; Endo S; Oda K; Saito K; Kunishima H; Hatta M; Inden K; Kaku M
CS Department of Infection Control and Laboratory Diagnostics, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aobaku, Sendai, Miyagi 980-8574, Japan.
SO The Journal of hospital infection, (2007 Jun) Vol. 66, No. 2, pp. 130-4. Electronic Publication: 2007-05-18.
Journal code: 8007166. ISSN: 0195-6701.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200708
ED Entered STN: 6 Jun 2007
Last Updated on STN: 18 Aug 2007
Entered Medline: 17 Aug 2007
AB Routine surveillance in a **cardiovascular** ward showed that the incidence of Enterobacter cloacae isolated from sputum and oropharyngeal cultures in June 2004 increased to 27.6% (8/29) compared to 5.5% (12/219) from the rest of the hospital during the same period (OR=13.2; 95% CI 2.97-58.7; P<0.05). While an increase in E. cloacae pneumonia was not verified, an investigation was undertaken by the infection control team to prevent an outbreak. The estimate of **relative risk** for E. cloacae infection was based on a case-control study which measured exposure to intubation, history of a stay in the intensive care unit (ICU) and oral care between patients with E. cloacae and those negative for E. cloacae. An odds ratio of 13.2 suggested cross-contamination via the transoesophageal echocardiography (TOE) probe in the ICU prior to transfer to the **cardiovascular** ward. Pulsed-field gel electrophoresis and antibiogram patterns were also consistent with this hypothesis. Intervention was undertaken in the form of enforcing the disinfection of TOE probes using a 0.55% phtharal solution and the use of a single-use sheath to protect the probe from recontamination. Following intervention, the incidence rate returned to previous levels. This report illustrates the limitations in the effectiveness of current nosocomial surveillance strategies due to the retrospective nature of analysis. Improved surveillance methods such as data-mining tools specifically applicable to the institution, patient population, region and country are needed to increase the sensitivity of detecting unrecognized outbreaks, including cross-contamination.

L2 ANSWER 9 OF 80 MEDLINE on STN

Full Text
AN 2007204997 MEDLINE
DN PubMed ID: 16702981
TI Antihypertensive therapy, the alpha-adducin polymorphism, and **cardiovascular** disease in high-**risk** hypertensive persons: the Genetics of Hypertension-Associated Treatment Study.
AU Davis B R; Arnett D K; Boerwinkle E; Ford C E; Leiendecker-Foster C; Miller M B; Black H; Eckfeldt J H
CS School of Public Health, University of Texas-Houston, Houston, TX 77030, USA.. barry.r.davis@uth.tmc.edu
SO The pharmacogenomics journal, (2007 Apr) Vol. 7, No. 2, pp. 112-22. Electronic Publication: 2006-05-16. Journal code: 101083949. ISSN: 1470-269X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL) (CLINICAL TRIAL)
LA English
FS Priority Journals
EM 200706
ED Entered STN: 6 Apr 2007
Last Updated on STN: 21 Jun 2007
Entered Medline: 20 Jun 2007
AB In a double-blind, outcome trial conducted in hypertensive patients randomized to chlorthalidone (C), amlodipine (A), lisinopril (L), or doxazosin (D), the alpha-adducin Gly460Trp polymorphism was typed (n=36 913). Mean follow-up was 4.9 years. **Relative risks** (RRs) of chlorthalidone versus other treatments were compared between **genotypes** (Gly/Gly+Gly/Trp versus Trp/Trp). Primary outcome was coronary heart disease (CHD). Coronary heart disease incidence did not differ among treatments or **genotypes** nor was there any interaction between treatment and **genotype** (P=0.660). Subgroup analyses indicated that Trp allele carriers had greater CHD **risk** with C versus A+L in women (RR=1.31) but not men (RR=0.91) with no RR gender differences for non-carriers (gender-gene-treatment interaction, P=0.002). The alpha-adducin gene is not an important modifier of antihypertensive treatment on **cardiovascular risk**, but women Trp allele carriers may have increased CHD **risk** if treated with C versus A or L. This must be confirmed to have implications for hypertension treatment.

L2 ANSWER 10 OF 80 MEDLINE on STN
Full Text
AN 2007061002 MEDLINE
DN PubMed ID: 17198546
TI **Risk** factors and myocardial infarction in patients with obstructive sleep apnea: impact of beta2-adrenergic receptor polymorphisms.
AU Bartels Nina K; Borgel Jan; Wieczorek Stefan; Buchner Nikolaus; Hanefeld Christoph; Bulut Daniel; Mugge Andreas; Rump Lars C; Sanner Bernd M; Epplen Jorg T
CS Human Genetics, Ruhr-University Bochum, Germany.. the_sirius@web.de
SO BMC medicine, (2007) Vol. 5, pp. 1. Electronic Publication: 2007-01-01. Journal code: 101190723. E-ISSN: 1741-7015.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200703
ED Entered STN: 2 Feb 2007
Last Updated on STN: 14 Mar 2007
Entered Medline: 13 Mar 2007
AB BACKGROUND: The increased sympathetic nervous activity in patients with obstructive sleep apnea (OSA) is largely responsible for the high prevalence of arterial hypertension, and it is suggested to adversely affect triglyceride and high-density lipoprotein (HDL) cholesterol levels in these patients. The functionally relevant polymorphisms of the beta2-adrenergic receptor (Arg-47Cys/Arg16Gly and Gln27Glu) have been shown to exert modifying effects on these **risk** factors in previous studies, but results are inconsistent. METHODS: We investigated a group of 429 patients (55 +/- 10.7 years; 361 men, 68 women) with moderate to severe obstructive sleep apnea (apnea/hypopnea index (AHI) 29.1 +/- 23.1/h) and, on average, a high **cardiovascular risk** profile (body mass

index 31.1 +/- 5.6, with hypertension in 60.1%, dyslipidemia in 49.2%, and diabetes in 17.2% of patients). We typed the beta2-adrenergic receptor polymorphisms and investigated the five most frequent haplotypes for their modifying effects on OSA-induced changes in blood pressure, heart rate, and lipid levels. The prevalence of **cardiovascular risk** factors and coronary heart disease (n = 55, 12.8%) and survived myocardial infarction (n = 27, 6.3%) were compared between the **genotypes** and haplotypes. RESULTS: Multivariate linear/logistic regressions revealed a significant and independent (from BMI, age, sex, presence of diabetes, use of antidiabetic, lipid-lowering, and antihypertensive medication) influence of AHI on daytime systolic and diastolic blood pressure, heart rate, prevalence of hypertension, and triglyceride and HDL levels. The beta2-adrenergic receptor **genotypes** and haplotypes showed no modifying effects on these relationships or on the prevalence of dyslipidemia, diabetes, and coronary heart disease, yet, for all three polymorphisms, heterozygous carriers had a significantly lower **relative risk** for myocardial infarction (Arg-47Cys: n = 195, odds ratio (OR) = 0.32, P = 0.012; Arg16Gly: n = 197, OR = 0.39, P = 0.031; Gln27Glu: OR = 0.37, P = 0.023). Carriers of the most frequent haplotype (n = 113) (haplotype 1; heterozygous for all three polymorphisms) showed a five-fold lower prevalence of survived myocardial infarction (OR = 0.21, P = 0.023). CONCLUSION: Our study showed no significant modifying effect of the functionally relevant beta2-adrenergic receptor polymorphisms on OSA-induced blood pressure, heart rate, or lipid changes. Nevertheless, heterozygosity of these polymorphisms is associated with a lower prevalence of survived myocardial infarction in this group with, on average, a high **cardiovascular risk** profile.

L2 ANSWER 11 OF 80 MEDLINE on STN
Full Text
AN 2007005509 MEDLINE
DN PubMed ID: 17174637
TI Absence of an interaction between the angiotensin-converting enzyme insertion-deletion polymorphism and pravastatin on **cardiovascular** disease in high-**risk** hypertensive patients: the Genetics of Hypertension-Associated Treatment (GenHAT) study.
AU Maitland-van der Zee Anke-Hilse; Boerwinkle Eric; Arnett Donna K; Davis Barry R; Leiendecker-Foster Catherine; Miller Michael B; Klungel Olaf H; Ford Charles E; Eckfeldt John H
CS School of Public Health, University of Texas Health Science Center at Houston, 1200 Hermann Pressler, Houston TX, USA.. a.h.maitland@pharm.uu.nl
SO American heart journal, (2007 Jan) Vol. 153, No. 1, pp. 54-8. Journal code: 0370465. E-ISSN: 1097-6744.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200701
ED Entered STN: 5 Jan 2007
Last Updated on STN: 26 Jan 2007
Entered Medline: 25 Jan 2007
AB BACKGROUND: The aim of this study was to determine whether the angiotensin-converting enzyme (ACE) insertion-deletion (ID) polymorphism interacts with pravastatin to modify the **risk** of coronary heart disease (CHD) and other **cardiovascular** end points in a large clinical trial. METHODS: GenHAT is an ancillary study of the ALLHAT. The ACE ID **genotyped** population in the lipid-lowering arm of ALLHAT included 9467 participants randomly assigned to pravastatin (n = 4741) or to usual care (n = 4726). The efficacy of pravastatin in reducing the **risk** of primary outcome (all-cause mortality) and secondary outcomes (fatal CHD and nonfatal myocardial infarction, **cardiovascular** disease [**CVD**] mortality, CHD, stroke, other **CVD**, non-**CVD** mortality, stroke, and heart failure) was compared between the **genotype** strata (dominant model ID + II vs DD, additive model II vs ID vs DD), by examining an interaction term in a Cox proportional hazards model. RESULTS: The **relative risk** of fatal CHD and nonfatal myocardial infarction among subjects randomized to pravastatin compared with subjects randomized to usual care was similar in subjects with the II **genotype** (hazard ratio [HR] 0.84, 95% CI 0.59-1.18), the ID **genotype** (HR 0.84, 95% CI 0.68-1.03), and the DD **genotype** (HR 0.99, 95% CI 0.77-1.27). CONCLUSIONS: We found no evidence that the ACE ID **genotype** was a major modifier of the efficacy of pravastatin in reducing the **risk** of **cardiovascular** events.

L2 ANSWER 12 OF 80 MEDLINE on STN
Full Text
AN 2006701501 MEDLINE
DN PubMed ID: 17139368
TI Incidence of venous thromboembolism in first-degree relatives of patients with venous thromboembolism who have factor V Leiden.
AU Couturaud Francis; Kearon Clive; Leroyer Christophe; Mercier Bernard; Abgrall Jean Francois; Le Gal Gregoire; Lacut Karine; Oger Emmanuel; Bressollette Luc; Ferec Claude; Lamure Michel; Mottier Dominique
CS GETBO, EA 3878, Department of Internal Medicine and Chest Diseases, University Hospital Centre La Cavale Blanche, 29609 Brest, Cedex, France. (Groupe d'Etude de la Thrombose de Bretagne Occidentale (G.E.T.B.O)). francis.couturaud@chu-brest.fr
SO Thrombosis and haemostasis, (2006 Dec) Vol. 96, No. 6, pp. 744-9. Journal code: 7608063. ISSN: 0340-6245.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200702
ED Entered STN: 2 Dec 2006
Last Updated on STN: 17 Feb 2007
Entered Medline: 16 Feb 2007
AB The factor V Leiden (FVL) mutation, a genetic abnormality with an autosomal mode of inheritance, is associated with an increased **risk** of venous thromboembolism (VTE). We aimed to determine the annual incidence of VTE in first-degree relatives of patients with VTE and FVL and to identify factors in patients and the relatives that influence this incidence. In this retrospective and prospective cohort study, the incidence of objectively diagnosed first episodes of VTE was assessed in 553 first-degree relatives of 161 patients with acute VTE and FVL. The annual incidence of VTE was 0.43% (95% CI, 0.3 to 0.56) with FVL and 0.17% (95% CI, 0.07 to 0.27) without FVL (**relative risk** of 2.5,95% CI, 1.3 to 4.7). A majority (70%) of episodes of VTE were provoked, and this proportion was similar with and without FVL. A larger proportion of VTE was provoked in women (83%) that in men (33%), with the difference accounted for by pregnancy and use of oral contraceptives. The proportion of pregnancies complicated by VTE was 3.9% (95% CI, 2.0-5.8) with FVL and 1.4% (95% CI, 0.04-2.7) without FVL. FVL is associated with a two- to threefold increase in VTE in first-degree relatives of patients with VTE. No subgroup of relatives was identified who require more than routine prophylaxis because of a particularly high **risk** of VTE.

L2 ANSWER 13 OF 80 MEDLINE on STN
Full Text
AN 2006665806 MEDLINE
DN PubMed ID: 17101823
TI Diabetes mellitus and **risk** of developing Alzheimer disease: results from the Framingham Study.
AU Akomolafe Abimbola; Beiser Alexa; Meigs James B; Au Rhoda; Green Robert C; Farrer Lindsay A; Wolf Philip A; Seshadri Sudha
CS Department of Medicine, Morehouse School of Medicine, Atlanta, GA, USA.
NC 3R01-AG09029 (United States NIA)
5R01-AG08122 (United States NIA)
5R01-AG16495 (United States NIA)
5R01-NS17950 (United States NINDS)
N01-HC-25195 (United States NHLBI)
P30 AG13846 (United States NIA)
SO Archives of neurology, (2006 Nov) Vol. 63, No. 11, pp. 1551-5. Journal code: 0372436. ISSN: 0003-9942.
CY United States
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200612
ED Entered STN: 15 Nov 2006
Last Updated on STN: 19 Dec 2006
Entered Medline: 12 Dec 2006

AB BACKGROUND: Diabetes mellitus (DM) could increase the **risk** of Alzheimer disease (AD) through several biologically plausible pathways, but the relationship between DM and the development of AD remains uncertain. OBJECTIVE: To compare the **risk** of developing AD in subjects with and without DM. DESIGN: Prospective community-based cohort study. PARTICIPANTS: Framingham Study Original cohort participants who were dementia free and attended the 16th biennial examination (n = 2210 persons, 1325 women; mean age, 70 years). MAIN OUTCOME MEASURES: **Relative risk** of incident AD (criteria from the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association) associated with baseline DM (casual plasma glucose >or=200 mg/dL [>or=11.1 mmol/L] or use of insulin or a hypoglycemic drug) in overall group and within subgroups defined by apolipoprotein E **genotype** and plasma homocysteine levels; models were adjusted for age, sex, and **cardiovascular risk** factors. RESULTS: At baseline, 202 participants (9.1%) had DM. During the follow-up period (mean, 12.7 years; range, 1-20 years), 17 of 202 persons with DM (8.4%) and 220 of 2008 persons without DM (11.0%) developed AD, yielding a **relative risk** of 1.15 (95% confidence interval, 0.65-2.05). Among subjects without an apolipoprotein E epsilon4 allele or elevated plasma homocysteine levels, 44 of 684 persons (6.4%) developed AD; **relative risk** for AD comparing diabetic patients with nondiabetic patients was 2.98 (95% confidence interval, 1.06-8.39; P = .03). The effect was strongest in persons aged 75 years or older with a **relative risk** of 4.77 (95% confidence interval, 1.28-17.72; P = .02). CONCLUSION: Diabetes mellitus did not increase the **risk** of incident AD in the Framingham cohort overall; however, DM may be a **risk** factor for AD in the absence of other known major AD **risk** factors.

L2 ANSWER 14 OF 80 MEDLINE on STN
Full Text
AN 2006639796 MEDLINE
DN PubMed ID: 17023672
TI TGF-beta 1 polymorphisms and **risk** of myocardial infarction and stroke: the Rotterdam Study.
AU Sie Mark P S; Uitterlinden Andre G; Bos Michiel J; Arp Pascal P; Breteler Monique M B; Koudstaal Peter J; Pols Huibert A P; Hofman Albert; van Duijn Cornelia M; Witteman Jacqueline C M
CS Department of Epidemiology and Biostatistics, Erasmus Medical Center, Rotterdam, PO Box 2040, 3000 CA Rotterdam, The Netherlands.
SO Stroke; a journal of cerebral circulation, (2006 Nov) Vol. 37, No. 11, pp. 2667-71. Electronic Publication: 2006-10-05.
Journal code: 0235266. E-ISSN: 1524-4628.
CY United States
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200611
ED Entered STN: 1 Nov 2006
Last Updated on STN: 15 Nov 2006
Entered Medline: 14 Nov 2006
AB BACKGROUND AND PURPOSE: Inflammation plays a pivotal role in the pathogenesis of atherosclerosis and of **cardiovascular** and cerebrovascular complications. Transforming growth factor-beta1 (TGF-beta1) is a pleiotropic cytokine with a central role in inflammation. Little is known of the relation of variations within the gene and **risk** of **cardiovascular** and cerebrovascular disease. We therefore investigated 5 polymorphisms in the TGF-beta1 gene (-800 G/A, -509 C/T, codon 10 Leu/Pro, codon 25 Arg/Pro, and codon 263 Thr/Ile) in relation to the **risk** of myocardial infarction and stroke in a population-based study. METHODS: Participants (N=6456) of the Rotterdam Study were included in the current study. Analyses of the relations of **genotypes** with the **risk** of myocardial infarction and stroke were performed according to Cox proportional-hazards methods. All analyses were adjusted for age, sex, conventional **cardiovascular risk** factors, and medical history. RESULTS: We found no association with the **risk** of myocardial infarction. A significantly increased **risk** of stroke was found, associated with the T allele of the -509 C/T polymorphism (**relative risk**, 1.26; (95% CI, 1.06 to 1.49) and the Pro variant of the codon 10 polymorphism (**relative risk**, 1.24; 95% CI, 1.04 to 1.48).

CONCLUSIONS: No association between the TGF-beta1 polymorphisms and myocardial infarction was observed; however, the -509 C/T and codon 10 Leu/Pro polymorphisms were associated with the **risk** of stroke.

L2 ANSWER 15 OF 80 MEDLINE on STN
Full Text
AN 2006596240 MEDLINE
DN PubMed ID: 16849409
TI A functional polymorphism in the glucocorticoid receptor gene and its relation to **cardiovascular** disease **risk** in familial hypercholesterolemia.
AU Koeijvoets Kristel C M C; van Rossum Elisabeth F C; Dallinga-Thie Geesje M; Steyerberg Ewout W; Defesche Joep C; Kastelein John J P; Lamberts Steven W J; Sijbrands Eric J G
CS Department of Internal Medicine, D435, Erasmus Medical Center, P.O. Box 2040, 3000 AC Rotterdam, The Netherlands.
SO The Journal of clinical endocrinology and metabolism, (2006 Oct) Vol. 91, No. 10, pp. 4131-6. Electronic Publication: 2006-07-18.
Journal code: 0375362. ISSN: 0021-972X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200611
ED Entered STN: 11 Oct 2006
Last Updated on STN: 14 Nov 2006
Entered Medline: 13 Nov 2006
AB CONTEXT: Individuals with the functional ER22/23EK variant in the glucocorticoid receptor gene are relatively resistant to the downstream consequences of glucocorticoids. Evidence suggests that carriers have a more favorable **cardiovascular risk** profile, but the relationship between this ER22/23EK variant and **cardiovascular** disease has not been hitherto assessed. OBJECTIVE: We, therefore, determined whether carriership of the ER22/23EK improves **cardiovascular** disease **risk** in patients with severe hypercholesterolemia. DESIGN, SETTING, AND PARTICIPANTS: In a multicenter cohort study, 2024 patients with heterozygous familial hypercholesterolemia, aged 18 yr and older, were **genotyped** for the ER22/23EK polymorphism. Patients were identified at lipid clinics throughout The Netherlands between 1989 and 2002. MAIN OUTCOME MEASURES: The primary outcome measure was **cardiovascular** disease. RESULTS: Seventy-six (7.8%) of 977 men and 72 (6.9%) of 1047 women were carriers of the ER22/23EK variant. A total of 395 men and 247 women had a **cardiovascular** event. In contrast to expected results, we observed no significant association of the ER22/23EK variant with **cardiovascular** disease **risk** (men: **relative risk**, 0.75; 95% confidence interval, 0.50-1.14; P = 0.2; women: **relative risk**, 1.37; 95% confidence interval, 0.82-2.28; P = 0.2). However, we found a significant interaction between gender and the polymorphism on **cardiovascular** disease (P = 0.02). CONCLUSIONS: In this large cohort of individuals with very high **risk** of **cardiovascular** disease, the association between the functional ER22/23EK polymorphism and **cardiovascular risk** was not significant overall, although it varied significantly by gender.

L2 ANSWER 16 OF 80 MEDLINE on STN
Full Text
AN 2006237048 MEDLINE
DN PubMed ID: 16645019
TI An insulin-like growth factor-I gene polymorphism modifies the **risk** of microalbuminuria in subjects with an abnormal glucose tolerance.
AU Rietveld I; Hofman A; Pols H A P; van Duijn C M; Lamberts S W J; Janssen J A M J L
CS Department of Internal Medicine, Rotterdam, The Netherlands.
SO European journal of endocrinology / European Federation of Endocrine Societies, (2006 May) Vol. 154, No. 5, pp. 715-21.
Journal code: 9423848. ISSN: 0804-4643.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200606
ED Entered STN: 29 Apr 2006

Last Updated on STN: 30 Jun 2006
Entered Medline: 29 Jun 2006

AB OBJECTIVE: Microalbuminuria (MA) is related to **cardiovascular** disease both in diabetic patients and non-diabetic subjects. DESIGN: We investigated whether a polymorphism near the promoter region of the IGF-I gene was related to the development of MA. METHODS: For this study, 1069 participants of the Rotterdam study were selected (440 participants with an abnormal glucose tolerance (AGT), 220 participants with type 2 diabetes and 254 subjects with pre-diabetes, and 595 subjects with a normal glucose tolerance (NGT). RESULTS: 787 subjects were carriers of the wild type IGF-I **genotype** (73.6%) and 282 subjects were variant carriers (26.4%) of this IGF-I gene polymorphism. Compared to subjects with NGT the **risk** for microalbuminuria was higher (Odds Ratio (OR): 3.1 (95% CI: 1.2-7.7); P = 0.02) in variant carriers with AGT than in carriers of the wild type of this IGF-I gene polymorphism (OR: 2.2 (95% CI: 1.2-4.0); P = 0.009). Compared with wild type carriers with AGT, the **relative risk** for MA was unadjusted and non-significantly increased in variant carriers with AGT (1.6; 95% CI: 0.8-2.9). However, after adjustment for possible confounding factors (age, gender, mean blood pressure, fasting insulin, fasting glucose and smoking) this **risk** became significant (OR: RR 2.1; 95% CI:1.1-4.4; P = 0.04). CONCLUSIONS: In subjects with AGT, a higher **risk** for MA was observed in variant carriers than in carriers of the wild type **genotype** of this IGF-I gene polymorphism. Since MA is primarily associated with **cardiovascular** disease in subjects with AGT, our study suggests that variant carriers have a higher **risk** for **cardiovascular** disease than carriers of the wild type when they develop an AGT.

L2 ANSWER 17 OF 80 MEDLINE on STN
Full Text
AN 2006033211 MEDLINE
DN PubMed ID: 16420195
TI Alcohol consumption and **risk** of coronary heart disease in older adults: the **Cardiovascular** Health Study.
AU Mukamal Kenneth J; Chung Hyoju; Jenny Nancy S; Kuller Lewis H; Longstreth W T Jr; Mittleman Murray A; Burke Gregory L; Cushman Mary; Psaty Bruce M; Siscovick David S
CS Division of General Medicine and Primary Care, Beth Israel Deaconess Medical Center, Boston, Massachusetts 02215, USA..
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NC N01-HC-15103 (United States NHLBI)
N01-HC-35129 (United States NHLBI)
N01-HC-85079 (United States NHLBI)
N01-HC-85080 (United States NHLBI)
N01-HC-85081 (United States NHLBI)
N01-HC-85082 (United States NHLBI)
N01-HC-85083 (United States NHLBI)
N01-HC-85084 (United States NHLBI)
N01-HC-85085 (United States NHLBI)
N01-HC-85086 (United States NHLBI)
SO Journal of the American Geriatrics Society, (2006 Jan) Vol. 54, No. 1, pp. 30-7.
Journal code: 7503062. ISSN: 0002-8614.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LA English
FS Priority Journals
EM 200604
ED Entered STN: 20 Jan 2006
Last Updated on STN: 8 Apr 2006
Entered Medline: 7 Apr 2006

AB OBJECTIVES: To evaluate several aspects of the relationship between alcohol use and coronary heart disease in older adults, including beverage type, mediating factors, and type of outcome. DESIGN: Prospective cohort study. SETTING: Four U.S. communities. PARTICIPANTS: Four thousand four hundred ten adults aged 65 and older free of **cardiovascular** disease at baseline. MEASUREMENTS: **Risk** of incident myocardial infarction or coronary death according to self-reported consumption of beer, wine, and spirits ascertained yearly. RESULTS: During an average follow-up period of 9.2 years, 675 cases of incident myocardial infarction or coronary death occurred. Compared with long-term abstainers, multivariate

relative risks of 0.90 (95% confidence interval (CI)=0.71-1.14), 0.93 (95% CI=0.73-1.20), 0.76 (95% CI=0.53-1.10), and 0.58 (95% CI=0.39-0.86) were found in consumers of less than one, one to six, seven to 13, and 14 or more drinks per week, respectively (P for trend=.007). Associations were similar for secondary coronary outcomes, including nonfatal and fatal events. No strong mediators of the association were identified, although fibrinogen appeared to account for 9% to 10% of the relationship. The associations were statistically similar for intake of wine, beer, and liquor and generally similar in subgroups, including those with and without an apolipoprotein E4 allele. CONCLUSION: In this population, consumption of 14 or more drinks per week was associated with the lowest **risk** of coronary heart disease, although clinicians should not recommend moderate drinking to prevent coronary heart disease based on this evidence alone, because current National Institute on Alcohol Abuse and Alcoholism guidelines suggest that older adults limit alcohol intake to one drink per day.

L2 ANSWER 18 OF 80 MEDLINE on STN
Full Text
AN 2006032628 MEDLINE
DN PubMed ID: 16375773
TI Cystathionine beta-synthase T833C/844INS68 polymorphism: a family-based study on mentally retarded children.
AU Dutta Samikshan; Sinha Swagata; Chattopadhyay Anindita; Gangopadhyay Prasanta Kumar; Mukhopadhyay Jotideb; Singh Manoranjan; Mukhopadhyay Kanchan
CS Manovikas Biomedical Research and Diagnostic Centre, E,M, Bypass, Kolkata, India.. mikpal2000@yahoo.com
SO Behavioral and brain functions : BBF, (2005) Vol. 1, pp. 25. Electronic Publication: 2005-12-26.
Journal code: 101245751. E-ISSN: 1744-9081.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; PUBMED-NOT-MEDLINE
EM 200707
ED Entered STN: 20 Jan 2006
Last Updated on STN: 12 Dec 2006
Entered Medline: 24 Jul 2007
AB BACKGROUND: Cystathionine beta-synthase (CBS) mediates conversion of homocysteine to cystathionine and deficiency in enzyme activity may lead to hyperhomocysteinemia/homocystinuria, which are often associated with mental retardation (MR). A large number of polymorphisms have been reported in the CBS gene, some of which impair its activity and among these, a T833C polymorphism in cis with a 68 bp insertion at 844 in the exon 8 is found to be associated with mild hyperhomocysteinemia in different ethnic groups. METHODS: The present study is aimed at investigating the association between T833C/844ins68 polymorphism and MR. One hundred and ninety MR cases were recruited after psychometric evaluation. Hundred and thirty-eight control subjects, two hundred and sixty-seven parents of MR probands and thirty **cardiovascular** disorder (**CVD**) patients were included for comparison. Peripheral blood was collected after obtaining informed written consent. The T833C/844ins68 polymorphism was investigated by PCR amplification of genomic DNA and restriction fragment length polymorphism analysis, followed by statistical analysis. RESULTS: The **genotypic** distribution of the polymorphism was within the Hardy-Weinberg equilibrium. A slightly increased **genotypic** frequency was observed in the Indian control population as compared to other Asian populations. Both haplotype-based haplotype **relative risk** analysis and transmission disequilibrium test reveled lack of association of the T833C/844ins68 polymorphism with MR; nevertheless, the **relative risk** calculated was higher (>1) and in a limited number of informative MR families, preferential transmission of the double mutant from heterozygous mothers to the MR probands was noticed (chi2 = 4.00, P < 0.05). CONCLUSION: This is the first molecular genetic study of CBS gene dealing with T833C/844ins68 double mutation in MR subjects. Our preliminary data indicate lack of association between T833C/844ins68 polymorphism with MR. However, higher **relative risk** and biased transmission of the double mutation from heterozygous mothers to MR probands are indicative of a **risk** of association between this polymorphism with mental retardation.

L2 ANSWER 19 OF 80 MEDLINE on STN
Full Text
AN 2005643479 MEDLINE
DN PubMed ID: 15899484
TI **Genotype** of the mutant LDL receptor allele is associated with LDL particle size heterogeneity in familial hypercholesterolemia.
AU Hogue Jean-Charles; Lamarche Benoit; Gaudet Daniel; Tremblay Andre J; Despres Jean-Pierre; Gagne Claude; Couture Patrick
CS Lipid Research Center (S-102), CHUL Research Center, Laval University, Que., G1V 4G2, Canada.
SO Atherosclerosis, (2006 Jan) Vol. 184, No. 1, pp. 163-70.
Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200604
ED Entered STN: 6 Dec 2005
Last Updated on STN: 12 Apr 2006
Entered Medline: 11 Apr 2006
AB Small, dense LDL particles have been associated with an increased **risk** of coronary artery disease. In order to assess the potential contribution of the **genotype** of the LDL receptor to LDL particle size heterogeneity in familial hypercholesterolemia (FH), we examined the electrophoretic characteristics of LDL particles in a large cohort of FH heterozygotes and controls. A total of 259 FH heterozygotes and 208 controls participated in the study. FH subjects were carriers of one of the nine French Canadian mutations in the LDL receptor gene. LDL particles were characterized by polyacrylamide gradient gel electrophoresis following a 6-week lipid-lowering drug-free baseline period. LDL-peak particle diameter (LDL-PPD), representing the most abundant LDL particle subpopulation, was significantly smaller in FH heterozygotes carrying a negative-receptor mutation than in subjects carrying a defective-receptor mutation (negative-receptor = 257.3 +/- 4.1 A versus defective-receptor = 259.0 +/- 4.3 A, p = 0.0006). No significant difference in plasma CETP concentrations was found between these two **genotypic** groups. Moreover, compared with controls having low triglyceride levels, negative-receptor subjects with high triglyceride levels had a **relative risk** of 19.6 (p < 0.0001) of having small, dense LDL particles while this **risk** was not significantly increased among defective-receptor subjects. Multivariate analysis showed that the LDL receptor status accounted for 5.7% of the variance in the LDL-PPD after adjustment for covariates. These results suggest that the **genotype** of the mutant LDL receptor allele was independently associated with variations in LDL-PPD and could partly explain why negative-receptor FH heterozygotes may be at greater **risk** of **cardiovascular** disease than defective-receptor FH subjects.

L2 ANSWER 20 OF 80 MEDLINE on STN
Full Text
AN 2005636076 MEDLINE
DN PubMed ID: 16316363
TI Effects of single-nucleotide polymorphisms in MTHFR and MTRR on mortality and allograft loss in kidney transplant recipients.
AU Winkelmayer Wolfgang C; Kramar Reinhard; Sunder-Plassmann Gere; Fodinger Manuela
CS Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Boston, MA 02120, USA.. wolfgang@post.harvard.edu
SO Kidney international, (2005 Dec) Vol. 68, No. 6, pp. 2857-62.
Journal code: 0323470. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200602
ED Entered STN: 1 Dec 2005
Last Updated on STN: 2 Feb 2006
Entered Medline: 1 Feb 2006
AB BACKGROUND: Plasma total homocysteine (tHcy) is associated with **cardiovascular** outcomes in kidney transplant recipients (KTR). The

methylenetetrahydrofolate-reductase (MTHFR) 677C>T polymorphism, an important determinant of plasma tHcy concentrations, could therefore constitute an important prognostic marker. METHODS: We prospectively followed 710 KTR over >6 years. The MTHFR677C>T, MTHFR1298A>C, MTHFR1793G>A, and MTRR66A>G polymorphisms were analyzed. Demographic, clinical, and transplant-related information was obtained, and patients were followed-up using the Austrian Dialysis and Transplant Registry. Using Cox regression, we established the independent relations of each **genotype** to the **risk** of death from any cause, and/or kidney allograft loss. RESULTS: During a median follow-up of 6.1 years, 154 participants died and 260 kidney allografts were lost. Compared to patients with the MTHFR677CC **genotype**, patients with MTHFR677CT had an adjusted relative mortality **risk** of 1.02 (95%CI 0.70-1.47), and those with MTHFR677TT of 0.98 (95%CI 0.52-1.85). Compared to MTHFR677CC, the **relative risks** of kidney allograft loss were 0.93 (95%CI 0.70-1.23; MTHFR677CT) and 0.78 (95%CI 0.47-1.30; MTHFR677TT), respectively. None of the other **genotypes** were associated with the **risks** studied, either. These findings did not depend on whether we controlled for tHcy levels. CONCLUSION: This study does not support the routine use of MTHFR or MTRR **genotyping** for prognostic evaluation or **risk**-stratification in kidney transplant recipients.

L2 ANSWER 21 OF 80 MEDLINE on STN
Full Text
AN 2005544492 MEDLINE
DN PubMed ID: 16198657
TI Impact of CYP2D6 **genotype** on adverse effects during treatment with metoprolol: a prospective clinical study.
AU Fux Richard; Morike Klaus; Prohmer Anne M T; Delabar Ursula; Schwab Matthias; Schaeffeler Elke; Lorenz Gernot; Gleiter Christoph H; Eichelbaum Michel; Kivisto Kari T
CS Abteilung Klinische Pharmakologie, Lehrbereich Allgemeinmedizin der Medizinischen Fakultat, and Koordinierungszentrum Klinische Studien, Universitatsklinikum Tubingen, Tubingen, Germany.
SO Clinical pharmacology and therapeutics, (2005 Oct) Vol. 78, No. 4, pp. 378-87.
Journal code: 0372741. ISSN: 0009-9236.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200511
ED Entered STN: 14 Oct 2005
Last Updated on STN: 3 Nov 2005
Entered Medline: 2 Nov 2005
AB OBJECTIVE: Our objective was to study the impact of the cytochrome P450 (CYP) 2D6 polymorphism on the tolerability of metoprolol in a real-life primary care setting. The adverse effects studied comprised effects related to the central nervous system, **cardiovascular** effects, and sexual dysfunction. METHODS: Patients in whom treatment with metoprolol was considered were enrolled into this prospective, 6-week multicenter study. The dosage of metoprolol was determined on an individual basis and could be freely adjusted on clinical grounds. The indication for treatment was hypertension in about 90% of cases. Systolic and diastolic blood pressure, resting heart rate, and plasma metoprolol and alpha-hydroxymetoprolol concentrations were measured. CYP2D6 **genotyping** covered alleles *3 to *10 and *41 and the duplications. Possible adverse effects of metoprolol were systematically assessed over a 6-week period by means of standardized rating scales and questionnaires. RESULTS: The final study population comprised 121 evaluable patients (all white patients); among them, there were 5 ultrarapid metabolizers (UMs) (4.1%), 91 extensive metabolizers (EMs) (75%), 21 intermediate metabolizers (IMs) (17%), and 4 poor metabolizers (PMs) (3.3%). Plasma metoprolol concentrations normalized for the daily dose and metoprolol/alpha-hydroxymetoprolol ratios at steady state were markedly influenced by CYP2D6 **genotype** and displayed a gene-dose effect. The median of the dose-normalized metoprolol concentration was 0.0088 ng/mL, 0.047 ng/mL, 0.34 ng/mL, and 1.34 ng/mL among UMs, EMs, IMs, and PMs, respectively (P<.0001). There was no significant association between

CYP2D6 **genotype**-derived phenotype (EMs and UMs combined versus PMs and IMs combined) and adverse effects during treatment with metoprolol. There was a tendency toward a more frequent occurrence of cold extremities in the PM plus IM group as compared with the EM plus UM group (16.0% versus 4.2%, P=.056; **relative risk**, 3.8 [95% confidence interval, 1.03--14.3]). CONCLUSIONS: CYP2D6 **genotype**-derived phenotype was not significantly associated with a propensity for adverse effects to develop during treatment with metoprolol. However, the results concerning tolerability of metoprolol in PMs were inconclusive because of the small number of PMs enrolled.

L2 ANSWER 22 OF 80 MEDLINE on STN
Full Text
AN 2005472081 MEDLINE
DN PubMed ID: 16139102
TI DNA polymorphisms in the tyrosine hydroxylase and GNB3 genes: association with unexpected death from acute myocardial infarction and increased heart weight.
AU Klintschar M; Stiller D; Schwaiger P; Kleiber M
CS Institute of Legal Medicine, Martin Luther University Halle-Wittenberg, Franzosenweg 1, D06112 Halle, Germany.. michael.klintschar@medizin.uni-halle.de
SO Forensic science international, (2005 Oct 29) Vol. 153, No. 2-3, pp. 142-6. Electronic Publication: 2004-11-06.
Journal code: 7902034. ISSN: 0379-0738.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200512
ED Entered STN: 7 Sep 2005
Last Updated on STN: 18 Dec 2005
Entered Medline: 13 Dec 2005
AB Sudden and unexpected death from myocardial infarction (MI) is one of the most commonly observed findings in forensic medicine. To investigate the biochemical and genetic background of this disease we investigated the **genotypes** for two polymorphisms associated with hypertension: TH01, a tetrameric microsatellite in the tyrosine hydroxylase gene and the single nucleotide polymorphism C825T in the GNB3 gene in 116 sudden deaths from MI (78 males, 38 females) and in a control group of 137 deaths from natural causes other than MI (52 males, 85 females). For TH01 no correlation with the prevalence of MI was found. For C825T, results were different. While for the male individuals allelic frequencies and **genotype** distributions were similar in both groups, T-homozygosity was significantly more common in female fatalities from MI than in the female control group (24% versus 7%; **Relative Risk** 2.29). Nevertheless, neither for TH01 nor for C825T an association with heart weight was found. Thus our results demonstrate that the C825T polymorphism may play a role in the development of myocardial infarctions, at least in females. They also demonstrate that the genetic component in complex diseases like MI may depend on the gender of the patients. As the influence of this polymorphism on arterial blood pressure appears to be relatively small, and G-proteins are involved in numerous intracellular signal cascades it can be speculated that T-homozygosity at this locus might influence the incidence or mortality of **cardiovascular** disease via hitherto unknown mechanisms.

L2 ANSWER 23 OF 80 MEDLINE on STN
Full Text
AN 2005454143 MEDLINE
DN PubMed ID: 16081863
TI Alcohol use and **risk** of ischemic stroke among older adults: the **cardiovascular** health study.
AU Mukamal Kenneth J; Chung Hyoju; Jenny Nancy S; Kuller Lewis H; Longstreth W T Jr; Mittleman Murray A; Burke Gregory L; Cushman Mary; Beauchamp Norman J Jr; Siscovick David S
CS Department of Medicine, Beth Israel Deaconess Medical Center, 330 Brookline Ave, Boston, MA 02215, USA.. kmukamal@bidmc.harvard.edu
NC N01 HC-15103 (United States NHLBI)
N01-HC-85079 (United States NHLBI)
N01-HC-85086 (United States NHLBI)
SO Stroke; a journal of cerebral circulation, (2005 Sep) Vol. 36, No. 9, pp.

1830-4. Electronic Publication: 2005-08-04.
Journal code: 0235266. E-ISSN: 1524-4628.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200601
ED Entered STN: 26 Aug 2005
Last Updated on STN: 13 Jan 2006
Entered Medline: 12 Jan 2006
AB BACKGROUND AND PURPOSE: The association of light to moderate alcohol consumption with **risk** of ischemic stroke remains uncertain, as are the roles of potentially mediating factors and modification by apolipoprotein E (apoE) **genotype**. METHODS: We studied the prospective association of alcohol consumption and **risk** of ischemic stroke among 4410 participants free of **cardiovascular** disease at baseline in the **Cardiovascular** Health Study, a population-based cohort study of older adults from 4 US communities. Participants reported their consumption of alcoholic beverages yearly. RESULTS: During an average follow-up period of 9.2 years, 434 cases of incident ischemic stroke occurred. Compared with long-term abstainers, the multivariate **relative risks** of ischemic stroke were 0.85 (95% CI, 0.63 to 1.13), 0.75 (95% CI, 0.53 to 1.06), 0.82 (95% CI, 0.51 to 1.30), and 1.03 (95% CI, 0.68 to 1.57) among consumers of <1, 1 to 6, 7 to 13, and > or =14 drinks per week (P quadratic trend 0.06). ApoE **genotype** appeared to modify the alcohol-ischemic stroke relationship (P interaction 0.08), with generally lower **risks** among drinkers than abstainers in apoE4-negative participants but higher **risks** among drinkers than abstainers among apoE4-positive participants. We could not identify candidate mediators among lipid, inflammatory, and prothrombotic factors. CONCLUSIONS: In this study of older adults, the association of alcohol use and **risk** of ischemic stroke was U-shaped, with modestly lower **risk** among consumers of 1 to 6 drinks per week. However, apoE **genotype** may modify this association, and even moderate alcohol intake may be associated with an increased **risk** of ischemic stroke among apoE4-positive older adults.

L2 ANSWER 24 OF 80 MEDLINE on STN
Full Text
AN 2005414284 MEDLINE
DN PubMed ID: 15890894
TI Reliable low-density DNA array based on allele-specific probes for detection of 118 mutations causing familial hypercholesterolemia.
AU Tejedor Diego; Castillo Sergio; Mozas Pilar; Jimenez Elisa; Lopez Monica; Tejedor M Teresa; Artieda Marta; Alonso Rodrigo; Mata Pedro; Simon Laureano; Martinez Antonio; Pocovi Miguel
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SO Clinical chemistry, (2005 Jul) Vol. 51, No. 7, pp. 1137-44. Electronic Publication: 2005-05-12.
Journal code: 9421549. ISSN: 0009-9147.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200508
ED Entered STN: 5 Aug 2005
Last Updated on STN: 17 Aug 2005
Entered Medline: 16 Aug 2005
AB BACKGROUND: Patients with familial hypercholesterolemia (FH) have a high **risk** of premature **cardiovascular** disease (PCVD). Mutations in the LDL receptor (LDLR) gene and the R3500Q mutation in the apolipoprotein B (APOB) gene are known to cause FH, but lack of high-throughput methods makes routine genetic diagnosis difficult. The objective of this work was to develop a DNA array for large-scale identification of mutant LDLR alleles. METHODS: We developed a low-density oligonucleotide microarray to identify 118 DNA sequence variations (117 for the LDLR gene and 1 for the APOB gene). We verified specificity and sensitivity by analyzing 1180 previously sequenced DNA samples, and conducted a blind study screening 407 Spanish patients with a clinical diagnosis of FH. RESULTS: The DNA

array confirmed the previous **genotyping** results in almost all cases. In the blind study, the microarray detected at least 1 mutation in 51% of the patients for whom clinical diagnosis was classified as certain according to Dutch FH-MEDPED criteria; it also identified mutations in 37% of those with a diagnosis of probable/possible FH, thus giving a definite diagnosis. Patients harboring null mutations had shorter PCVD-free survival times and higher **relative risk** of PCVD than patients with a missense mutation. CONCLUSIONS: The proposed DNA array allows large-scale population screening and provides molecular information regarding mutation type and its correlation with clinical severity of FH, which can be used to develop therapeutic strategies.

L2 ANSWER 25 OF 80 MEDLINE on STN
Full Text
AN 2005394958 MEDLINE
DN PubMed ID: 15920035
TI Peroxisome proliferator-activated receptor-gamma2 P12A polymorphism and **risk** of coronary heart disease in US men and women.
AU Pischon Tobias; Pai Jennifer K; Manson JoAnn E; Hu Frank B; Rexrode Kathryn M; Hunter David; Rimm Eric B
CS Department of Nutrition and Epidemiology, Harvard School of Public Health, Boston, Mass, USA.. pischon@mail.dife.de
NC CA55075 (United States NCI)
HL07575 (United States NHLBI)
HL34594 (United States NHLBI)
HL35464 (United States NHLBI)
SO Arteriosclerosis, thrombosis, and vascular biology, (2005 Aug) Vol. 25, No. 8, pp. 1654-8. Electronic Publication: 2005-05-26.
Journal code: 9505803. E-ISSN: 1524-4636.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200512
ED Entered STN: 2 Aug 2005
Last Updated on STN: 30 Dec 2005
Entered Medline: 29 Dec 2005
AB OBJECTIVE: Activation of the peroxisome proliferator-activated receptor-gamma (PPARgamma) improves insulin sensitivity and exerts antiatherogenic effects. A common alanine for proline substitution at codon 12 in the PPARG2 gene is related to lower receptor activity. Studies suggest that the A12 allele is associated with reduced **risk** of type 2 diabetes; however, data on the **risk** of coronary heart disease (CHD) are scarce and controversial. METHODS AND RESULTS: We examined the relationship between PPARG2 P12A and CHD **risk** in women (Nurses' Health Study) and men (Health Professionals Follow-Up Study) in nested case control settings. Among participants free of **cardiovascular** disease at baseline, 249 women and 266 men developed nonfatal myocardial infarction (MI) or fatal CHD during 8 and 6 years of follow-up, respectively. Using **risk**-set sampling, controls were selected 2:1 matched on age, smoking, and date of blood draw. The **relative risk** (RR) of nonfatal MI or fatal CHD of carriers compared with noncarriers of the A12 allele was 1.17 (95% CI, 0.82 to 1.68) among women and 1.44 (95% CI, 1.00 to 2.07) among men (pooled RR, 1.30 [95% CI, 1.00 to 1.67]). We found a significantly increased **risk** associated with the A12 allele among individuals with a body mass index > or =25 kg/m2 (women: RR, 1.88; 95% CI, 1.01 to 3.50; men: RR, 1.55; 95% CI, 0.92 to 2.60; pooled: RR, 1.68; 95% CI, 1.13 to 2.50) but not among those <25 kg/m2 (pooled RR, 0.86; 95% CI, 0.37 to 1.97; P heterogeneity overweight versus nonoverweight 0.16). CONCLUSIONS: These data do not support the hypothesis that the A12 allele is associated with a decreased **risk** of CHD. The potential interaction between PPARG2 P12A, overweight, and increased CHD **risk** needs further evaluation.

L2 ANSWER 26 OF 80 MEDLINE on STN
Full Text
AN 2005331650 MEDLINE
DN PubMed ID: 15967849
TI Pharmacogenetic association of the angiotensin-converting enzyme insertion/deletion polymorphism on blood pressure and **cardiovascular**

risk in relation to antihypertensive treatment: the Genetics of Hypertension-Associated Treatment (GenHAT) study.
AU Arnett Donna K; Davis Barry R; Ford Charles E; Boerwinkle Eric; Leiendecker-Foster Cathie; Miller Michael B; Black Henry; Eckfeldt John H
CS University of Minnesota, Division of Epidemiology, Minneapolis, USA.. arnett@ms.soph.uab.edu
NC 5 R01 HL-63082 (United States NHLBI)
SO Circulation, (2005 Jun 28) Vol. 111, No. 25, pp. 3374-83. Electronic Publication: 2005-06-20.
Journal code: 0147763. E-ISSN: 1524-4539.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
(CLINICAL TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200602
ED Entered STN: 29 Jun 2005
Last Updated on STN: 4 Feb 2006
Entered Medline: 3 Feb 2006
AB BACKGROUND: Previous studies have reported that blood pressure response to antihypertensive medications is influenced by genetic variation in the renin-angiotensin-aldosterone system, but no clinical trails have tested whether the ACE insertion/deletion (I/D) polymorphism modifies the association between the type of medication and multiple **cardiovascular** and renal phenotypes. METHODS AND RESULTS: We used a double-blind, active-controlled randomized trial of antihypertensive treatment that included hypertensives > or =55 years of age with > or =1 **risk** factor for **cardiovascular** disease. ACE I/D **genotypes** were determined in 37 939 participants randomized to chlorthalidone, amlodipine, lisinopril, or doxazosin treatments and followed up for 4 to 8 years. Primary outcomes included fatal coronary heart disease (CHD) and/or nonfatal myocardial infarction. Secondary outcomes included stroke, all-cause mortality, combined CHD, and combined **cardiovascular** disease. Fatal and nonfatal CHD occurred in 3096 individuals during follow-up. The hazard rates for fatal and nonfatal CHD and the secondary outcomes were similar across antihypertensive treatments. ACE I/D **genotype** group was not associated with fatal and nonfatal CHD (**relative risk** of DD versus ID and II, 0.99; 95% CI, 0.91 to 1.07) or any secondary outcome. The 6-year hazard rate for fatal and nonfatal CHD in the DD **genotype** group was not statistically different from the ID and II **genotype** group by type of treatment. No secondary outcome measure was statistically different across antihypertensive treatment and ACE I/D **genotype** strata. CONCLUSIONS: ACE I/D **genotype** group was not a predictor of CHD, nor did it modify the response to antihypertensive treatment. We conclude that the ACE I/D polymorphism is not a useful marker to predict antihypertensive treatment response.

L2 ANSWER 27 OF 80 MEDLINE on STN
Full Text
AN 2005323015 MEDLINE
DN PubMed ID: 15856070
TI TaqIB polymorphism in CETP gene: the influence on incidence of **cardiovascular** disease in statin-treated patients with familial hypercholesterolemia.
AU Mohrschladt Martina F; van der Sman-de Beer Femke; Hofman Maaike K; van der Krabben Marieke; Westendorp Rudi Gj; Smelt August Hm
CS Department of General Internal Medicine, Leiden University Medical Center, PO Box 9600, 2300 RC Leiden, The Netherlands.
SO European journal of human genetics : EJHG, (2005 Jul) Vol. 13, No. 7, pp. 877-82.
Journal code: 9302235. ISSN: 1018-4813.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200509
ED Entered STN: 24 Jun 2005
Last Updated on STN: 14 Sep 2005

Entered Medline: 13 Sep 2005

AB The effects of TaqI restriction fragment length polymorphism of the CETP gene on the occurrence of **cardiovascular** disease (**CVD**) events were investigated in patients with familial hypercholesterolemia (FH). A total of 300 FH patients, of which 116 (39%) had **CVD** at the start of the study, were treated with statins during a mean period of 8.5 years. The distribution of Taq1B **genotypes** was 31% B1B1, 49% B1B2, and 20% B2B2. No differences were found at baseline between the three **genotypes**, except for an association of the B1 allele with lower high-density lipoprotein (HDL)-cholesterol levels (P=0.003). All patients were put on statins within 6-8 weeks after the first visit; about 60% received simvastatin (20-40 mg daily) and 40% either pravastatin (40 mg daily) or atorvastatin (20-40 mg daily). The different statin treatments were similar for all groups. The mean change of plasma HDL-cholesterol, low-density lipoprotein-cholesterol, and triglyceride concentration during statin therapy was similar for the three **genotypes**. During follow-up, new **CVD** events were recorded in 22 (37%) of the B2B2 patients (n=59) and in 67 (28%) of B1 allele carriers (n=241) (P=0.36). The **relative risk** for **CVD** events, after adjustment for age, gender, and **CVD** at intake, was 1.8 (CI: 1.1-3.0) for B2B2 carriers compared to B1 allele carriers. The Taq1B polymorphism is a significant predictor of future **CVD** events in statin-treated patients with FH. In spite of similar improvement of the lipoprotein profile during statin therapy, our FH patients with the B2B2 **genotype** may have a higher **CVD risk** in comparison with the B1 allele carriers.

L2 ANSWER 28 OF 80 MEDLINE on STN

Full Text

AN 2005200594 MEDLINE

DN PubMed ID: 15833936

TI E-selectin **genotypes** and **risk** of type 2 diabetes in women.

AU Meigs James B; Hu Frank B; Perhanidis Jessica S; Hunter David; Rifai Nader; Manson Joann E

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NC CA87969 (United States NCI)
DK36798 (United States NIDDK)
DK46519 (United States NIDDK)
DK58845 (United States NIDDK)

SO Obesity research, (2005 Mar) Vol. 13, No. 3, pp. 513-8.
Journal code: 9305691. ISSN: 1071-7323.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LA English

FS Priority Journals

EM 200508

ED Entered STN: 19 Apr 2005
Last Updated on STN: 3 Aug 2005
Entered Medline: 2 Aug 2005

AB Endothelial dysfunction increases **risk** for type 2 diabetes. We examined whether variation in the gene for E-selectin (SELE), a biomarker of endothelial dysfunction, was associated with levels of E-selectin or diabetes quantitative traits (including fasting levels of insulin and hemoglobin A(1c)) in 719 nondiabetic participants of the Nurses' Health Study or with **risk** of diabetes in 602 incident (over 10 years of follow-up) cases and 655 control women matched for age, race, and fasting status. Variation in three single nucleotide polymorphisms previously associated with **cardiovascular** disease **risk** and having effects on E-selectin function, S128R, G98T, and L554F, was not significantly ($p > 0.05$) associated with levels of E-selectin or diabetes quantitative traits, or with **risk** of incident diabetes in the primary analysis. Among women with low levels of subclinical inflammation (C-reactive protein levels below the population median), S128R R allele carriers had a diabetes **risk** factor-adjusted **relative risk** of incident diabetes of 1.71 (95% confidence interval, 1.04 to 2.81) relative to those with the SS **genotype**. Apart from an association in this subgroup, we conclude that the E-selectin variants we examined are not important genetic **risk** factors for type 2 diabetes in women.

L2 ANSWER 29 OF 80 MEDLINE on STN
Full Text
AN 2005148054 MEDLINE
DN PubMed ID: 15781953
TI Physical activity, APOE **genotype**, and dementia **risk**: findings from the **Cardiovascular** Health Cognition Study.
AU Podewils Laura Jean; Guallar Eliseo; Kuller Lewis H; Fried Linda P; Lopez Oscar L; Carlson Michelle; Lyketsos Constantine G
CS Department of Epidemiology, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA.
NC AG15928 (United States NIA)
N01-HC-15103 (United States NHLBI)
N01-HC-35129 (United States NHLBI)
N01-HC-85079 (United States NHLBI)
N01-HC-85080 (United States NHLBI)
N01-HC-85081 (United States NHLBI)
N01-HC-85082 (United States NHLBI)
N01-HC-85083 (United States NHLBI)
N01-HC-85084 (United States NHLBI)
N01-HC-85085 (United States NHLBI)
N01-HC-85086 (United States NHLBI)
SO American journal of epidemiology, (2005 Apr 1) Vol. 161, No. 7, pp. 639-51.
Journal code: 7910653. ISSN: 0002-9262.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200505
ED Entered STN: 23 Mar 2005
Last Updated on STN: 13 May 2005
Entered Medline: 12 May 2005
AB Physical activity may help preserve cognitive function and decrease dementia **risk**, but epidemiologic findings are inconsistent. The authors conducted a prospective study to determine the association between physical activity and **risk** of dementia, Alzheimer's disease, and vascular dementia. The US study population comprised 3,375 men and women aged 65 years or older, free of dementia at baseline, who participated in the **Cardiovascular** Health Cognition Study in 1992-2000. Leisure-time energy expenditure and an activity index reflecting number of different physical activities were calculated. Analyses were based on Cox proportional hazards models. There were 480 incident cases of dementia over an average of 5.4 years of follow-up. After multivariate adjustment, participants in the highest quartile of physical energy expenditure had a **relative risk** of dementia of 0.85 (95% confidence interval: 0.61, 1.19) compared with those in the lowest quartile, and participants engaging in >or=4 activities had a **relative risk** of dementia of 0.51 (95% confidence interval: 0.33, 0.79) compared with those engaging in 0-1 activity. These associations were more marked in apolipoprotein E **genotype** (APOE) epsilon4 allele noncarriers but were absent in carriers. A similar pattern was observed for Alzheimer's disease and vascular dementia. Mechanisms to explain the observed relations deserve further study.

L2 ANSWER 30 OF 80 MEDLINE on STN
Full Text
AN 2005115337 MEDLINE
DN PubMed ID: 15677572
TI Association between a functional variant of the KLOTHO gene and high-density lipoprotein cholesterol, blood pressure, stroke, and longevity.
AU Arking Dan E; Atzmon Gil; Arking Albert; Barzilai Nir; Dietz Harry C
CS McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, Md 21205, USA.
NC DK 20541 (United States NIDDK)
M01-RR12248 (United States NCRR)
MH070172 (United States NIMH)
P01 AG-03949-01A1 (United States NIA)
R01 AG-18728-01A1 (United States NIA)
SO Circulation research, (2005 Mar 4) Vol. 96, No. 4, pp. 412-8. Electronic Publication: 2005-01-27.

Journal code: 0047103. E-ISSN: 1524-4571.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200508
ED Entered STN: 5 Mar 2005
Last Updated on STN: 26 Aug 2005
Entered Medline: 25 Aug 2005
AB We previously identified a functional variant of KLOTHO, termed KL-VS, that is associated with human aging and early-onset occult coronary artery disease. Here, we determine whether the KL-VS allele influences **cardiovascular** disease **risk** factors, **cardiovascular** events, and ultimately, mortality. A total of 525 Ashkenazi Jews composed of 216 probands (age > or =95 years) and 309 unrelated individuals (ages 51 to 94) were **genotyped** for the KL-VS allele. In concordance with our previous data in Czech individuals (age > or =79; P<0.01), a heterozygous advantage for longevity was observed for individuals > or =79 years of age (P<0.004). Combined analysis indicates a 1.57-fold (95% CI, 1.23 to 1.98) increased odds ratio (OR) for 5-year survival in two independent populations (P<0.0002). **Cardiovascular** disease **risk** factors were assessed through multivariate regression analysis, demonstrating that high-density lipoprotein cholesterol (HDL-C; P<0.05) and systolic blood pressure (SBP; P<0.008) are associated with KL-VS **genotype**. History of vascular events was analyzed using logistic regression, indicating that after adjustment for traditional **risk** factors, heterozygous individuals were at significantly lower **risk** for stroke than wild-type individuals (OR, 5.88; 95% CI, 1.18 to 29.41), whereas homozygous KL-VS individuals had the highest **risk** (OR, 30.65; 95% CI, 2.55 to 368.00). Similarly, prospective analysis of mortality in probands using Cox regression indicates that wild-type individuals have a 2.15-fold (95% CI, 1.18 to 3.91) and homozygous KL-VS individuals a 4.49-fold (95% CI, 1.35 to 14.97) increase in **relative risk** for mortality after adjusting for potential confounders. Thus, cross-sectional and prospective studies confirm a genetic model in which the KL-VS allele confers a heterozygous advantage in conjunction with a marked homozygous disadvantage for HDL-C levels, SBP, stroke, and longevity.

L2 ANSWER 31 OF 80 MEDLINE on STN
Full Text
AN 2005068552 MEDLINE
DN PubMed ID: 15640973
TI Association between the gene encoding 5-lipoxygenase-activating protein and stroke replicated in a Scottish population.
AU Helgadottir A; Gretarsdottir S; St Clair D; Manolescu A; Cheung J; Thorleifsson G; Pasdar A; Grant S F A; Whalley L J; Hakonarson H; Thorsteinsdottir U; Kong A; Gulcher J; Stefansson K; MacLeod M J
CS deCODE Genetics, Reykjavik, Iceland.
SO American journal of human genetics, (2005 Mar) Vol. 76, No. 3, pp. 505-9.
Electronic Publication: 2005-01-07.
Journal code: 0370475. ISSN: 0002-9297.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS OMIM-603700
EM 200503
ED Entered STN: 9 Feb 2005
Last Updated on STN: 29 Mar 2005
Entered Medline: 28 Mar 2005
AB **Cardiovascular** diseases, including myocardial infarction (MI) and stroke, most often occur on the background of atherosclerosis, a condition attributed to the interactions between multiple genetic and environmental **risk** factors. We recently reported a linkage and association study of MI and stroke that yielded a genetic variant, HapA, in the gene encoding 5-lipoxygenase-activating protein (ALOX5AP), that associates with both diseases in Iceland. We also described another ALOX5AP variant, HapB, that associates with MI in England. To further assess the contribution of the ALOX5AP variants to **cardiovascular** diseases in a population outside

Iceland, we **genotyped** seven single-nucleotide polymorphisms that define both HapA and HapB from 450 patients with ischemic stroke and 710 controls from Aberdeenshire, Scotland. The Icelandic at-**risk** haplotype, HapA, had significantly greater frequency in Scottish patients than in controls. The carrier frequency in patients and controls was 33.4% and 26.4%, respectively, which resulted in a **relative risk** of 1.36, under the assumption of a multiplicative model (P=.007). We did not detect association between HapB and ischemic stroke in the Scottish cohort. However, we observed that HapB was overrepresented in male patients. This replication of haplotype association with stroke in a population outside Iceland further supports a role for ALOX5AP in **cardiovascular** diseases.

L2 ANSWER 32 OF 80 MEDLINE on STN
Full Text
AN 2005006402 MEDLINE
DN PubMed ID: 15632091
TI Identification of polymorphic motifs using probabilistic search algorithms.
AU Basu Analabha; Chaudhuri Probal; Majumder Partha P
CS Human Genetics Unit, Indian Statistical Institute, Kolkata, 700108 India.
SO Genome research, (2005 Jan) Vol. 15, No. 1, pp. 67-77.
Journal code: 9518021. ISSN: 1088-9051.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200504
ED Entered STN: 6 Jan 2005
Last Updated on STN: 15 Apr 2005
Entered Medline: 14 Apr 2005
AB The problem of identifying motifs comprising nucleotides at a set of polymorphic DNA sites, not necessarily contiguous, arises in many human genetic problems. However, when the sites are not contiguous, no efficient algorithm exists for polymorphic motif identification. A search based on complete enumeration is computationally inefficient. We have developed probabilistic search algorithms to discover motifs of known or unknown lengths. We have developed statistical tests of significance for assessing a motif discovery, and a statistical criterion for simultaneously estimating motif length and discovering it. We have tested these algorithms on various synthetic data sets and have shown that they are very efficient, in the sense that the "true" motifs can be detected in the vast majority of replications and in a small number of iterations. Additionally, we have applied them to some real data sets and have shown that they are able to identify known motifs. In certain applications, it is pertinent to find motifs that contain contrasting nucleotides at the sites included in the motif (e.g., motifs identified in case-control association studies). For this, we have suggested appropriate modifications. Using simulations, we have discovered that the success rate of identification of the correct motif is high in case-control studies except when **relative risks** are small. Our analyses of evolutionary data sets resulted in the identification of some motifs that appear to have important implications on human evolutionary inference. These algorithms can easily be implemented to discover motifs from multilocus **genotype** data by simple numerical recoding of **genotypes**.

L2 ANSWER 33 OF 80 MEDLINE on STN
Full Text
AN 2005005039 MEDLINE
DN PubMed ID: 15630497
TI The plasminogen activator inhibitor (PAI-1) 4G/5G promoter polymorphism and PAI-1 levels in ischemic stroke. A case-control study.
AU van Goor Mary-Lou; Garcia Encarna Gomez; Leebeek Frank; Brouwers Geert-Jan; Koudstaal Peter; Dippel Diederik
CS Erasmus Medical Center Rotterdam, Department of Neurology, PO Box 2040, 3000 CA Rotterdam, The Netherlands.. m.vangoor@erasmusmc.nl
SO Thrombosis and haemostasis, (2005 Jan) Vol. 93, No. 1, pp. 92-6.
Journal code: 7608063. ISSN: 0340-6245.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English

FS Priority Journals
EM 200507
ED Entered STN: 5 Jan 2005
Last Updated on STN: 6 Jul 2005
Entered Medline: 5 Jul 2005
AB High levels of plasminogen activator inhibitor type 1 (PAI-1) have been implicated as a **risk** factor for **cardiovascular** disease, but its precise role remains controversial. The 4G allele of the PAI-1 4G/5G promoter polymorphism is associated with higher levels of PAI-1. We studied the relationship between ischemic stroke and the PAI-1 4G/5G polymorphism and PAI-1 antigen levels. We performed a case-control study among patients aged 18-75 years with first ischemic stroke, confirmed by CT. All patients were screened for **cardiovascular risk** factors, cardiac disorders and large vessel disease. We excluded patients with a definite non-atherosclerotic cause of the stroke and patients using oral anticoagulants. Population-controls were age -and sex-matched, without a history of stroke, and of the Caucasian race. Venous blood samples were taken for PAI-1 4G/5G polymorphism and PAI-1 level one week after stroke. We included 124 patients and 125 controls. Mean age was 56 yrs (range 18 to 75 yrs). Sixty one patients (50%) and 58 (47%) controls were heterozygous for the PAI-1 4G/5G polymorphism. The homozygous 4G/4G **genotype** was found in 33 patients (27%) and in 36 controls (29%). The odds ratio of ischemic stroke associated with 4G-carriers versus 5G/5G homozygotes was 1.0 (95% CI: 0.6-1.8). The **relative risk** of ischemic stroke associated with the level of PAI-1 in the upper quartile was 0.73 (95%CI: 0.4 to 1.4). Neither the PAI-1 4G/5G polymorphism nor the PAI-1 antigen level is a strong **risk** factor for ischemic stroke.

L2 ANSWER 34 OF 80 MEDLINE on STN
Full Text
AN 2004518064 MEDLINE
DN PubMed ID: 15241484
TI Effect of genetic variation in the human S-adenosylhomocysteine hydrolase gene on total homocysteine concentrations and **risk** of recurrent venous thrombosis.
AU Gellekink Henkjan; den Heijer Martin; Kluijtmans Leo A J; Blom Henk J
CS Laboratory of Pediatrics and Neurology, University Medical Center Nijmegen, The Netherlands.
SO European journal of human genetics : EJHG, (2004 Nov) Vol. 12, No. 11, pp. 942-8.
Journal code: 9302235. ISSN: 1018-4813.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200505
ED Entered STN: 19 Oct 2004
Last Updated on STN: 12 May 2005
Entered Medline: 11 May 2005
AB Hyperhomocysteinemia is an independent and graded **risk** factor for arterial vascular disease and venous thrombosis. It is still debated via which mechanism homocysteine (Hcy) causes vascular disease. S-adenosylhomocysteine hydrolase (AHCY) catalyses the reversible hydrolysis of S-adenosylhomocysteine (AdoHcy) to Hcy. As an increase in AdoHcy, a strong inhibitor of many methyltransferases, is observed in hyperhomocysteinemic individuals, AdoHcy may play a role in the development of **cardiovascular** diseases by inhibiting transmethylation reactions. We sequenced the entire coding region and parts of the untranslated regions (UTRs) of the AHCY gene of 20 patients with recurrent venous thrombosis in order to identify genetic variation within this gene. We identified three sequence variants in the AHCY gene: a C > T transition in the 5' UTR (-34 bp C > T), a missense mutation in exon 2, which mandates an amino-acid conversion at codon 38 (112 C > T; Arg38Trp) and a silent mutation in exon 4 (390 C > T; Asp130Asp). We studied the effect of the first two variants on total plasma Hcy and venous thrombosis **risk** in a case-control study on recurrent venous thrombosis. The two polymorphisms under study seem to have no evident effect on tHcy. The adjusted **relative risk** of venous thrombosis associated with the 112CT **genotype** compared with 112CC individuals was 1.27 (95% CI 0.55-2.94), whereas the -34CT **genotype** confers a **risk** of 1.25 (95% CI 0.44-3.52) compared with the wild-type **genotype** at this locus. However, the wide

confidence intervals do not allow firm conclusions to be drawn.

L2 ANSWER 35 OF 80 MEDLINE on STN
Full Text
AN 2004467243 MEDLINE
DN PubMed ID: 15377476
TI G20210A prothrombin gene variant and clinical outcome in patients with a first acute coronary syndrome.
AU Burzotta Francesco; Leone Antonio Maria; Paciaroni Katia; De Stefano Valerio; Rossi Elena; Testa Luca; Giannico Floriana; Leone Giuseppe; Maseri Attilio; Crea Filippo; Andreotti Felicita
CS Institute of Cardiology, Catholic University, Rome, Italy.. f.burzotta@eudoramail.com
SO Haematologica, (2004 Sep) Vol. 89, No. 9, pp. 1134-8.
Journal code: 0417435. E-ISSN: 1592-8721.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200604
ED Entered STN: 21 Sep 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 26 Apr 2006
AB BACKGROUND AND OBJECTIVES: The prognostic value of the G20210A prothrombin gene polymorphism in patients with a first acute coronary syndrome has not been previously assessed. We conducted a prospective study to investigate this issue. DESIGN AND METHODS: **Genotyping** at the 20210 prothrombin gene locus was performed in 162 patients with a first episode of myocardial infarction (MI) or unstable angina (UA) occurring before 65 years of age. Patients were stratified according to **cardiovascular risk** factors and to treatment strategy. The subsequent two-year **relative risk** (RR) of adverse events (death, MI and UA) was adjusted for possible confounders and analyzed according to **genotype**, **risk** factor category, and treatment allocation. RESULTS: In the entire study population, the prothrombin variant did not significantly increase the two-year **risk** of events: the adjusted RR for GA vs GG carriers was 1.82 (95% CI 0.68-4.89). However, in the absence of traditional **cardiovascular risk** factors the **risk** of events was consistently higher: among the 46 patients without hypertension, diabetes and hypercholesterolemia, GA vs GG carriership was associated with an adjusted RR at two years of 5.64 (95% CI 1.07-29.84). The gene variant also enhanced the **risk** of events among the 98 patients who did not undergo myocardial revascularization procedures (RR for GA vs GG: 2.89, 95% CI 1.04-8.00), but not among those who did. INTERPRETATION AND CONCLUSIONS: The present prospective study suggests that heterozygosity for the G20210A prothrombin polymorphism adversely affects prognosis after a first acute coronary syndrome in the subgroup of patients without metabolic **risk** factors and in those not treated by revascularization procedures.

L2 ANSWER 36 OF 80 MEDLINE on STN
Full Text
AN 2004461430 MEDLINE
DN PubMed ID: 15282206
TI A common haplotype at the CD36 locus is associated with high free fatty acid levels and increased **cardiovascular risk** in Caucasians.
AU Ma Xiaowei; Bacci Simonetta; Mlynarski Wojciech; Gottardo Lucia; Soccio Teresa; Menzaghi Claudia; Iori Elisabetta; Lager Robert A; Shroff Adhir R; Gervino Ernest V; Nesto Richard W; Johnstone Michael T; Abumrad Nada A; Avogaro Angelo; Trischitta Vincenzo; Doria Alessandro
CS Research Division, Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA.
NC DK36836 (United States NIDDK)
DK60837 (United States NIDDK)
HL71981 (United States NHLBI)
HL73168 (United States NHLBI)
SO Human molecular genetics, (2004 Oct 1) Vol. 13, No. 19, pp. 2197-205.
Electronic Publication: 2004-07-28.
Journal code: 9208958. ISSN: 0964-6906.
CY England: United Kingdom
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200502
ED Entered STN: 17 Sep 2004
Last Updated on STN: 18 Feb 2005
Entered Medline: 17 Feb 2005
AB CD36 is a class B scavenger receptor recognizing a variety of ligands including long-chain fatty acids and modified LDL. We investigated whether genetic variability at this locus is a determinant of free fatty acid (FFA) plasma levels and **risk** of coronary artery disease (CAD) in Caucasians. Typing of 21 polymorphic markers, evenly spanning the CD36 gene, revealed two linkage disequilibrium (LD) blocks that could be tagged by five polymorphisms (-33137A>G, -31118G>A, 25444G>A, 27645del>ins and 30294G>C). In 585 non-diabetic individuals of Caucasian origin, the 30294G>C polymorphism was significantly associated with FFA levels (P = 0.02)--an effect that was especially visible among men (P = 0.009). A similar association was observed in this gender at -33137 (P = 0.008) and -31118 (P = 0.028). When the five tag polymorphisms were considered together, men carrying the AGGIG haplotype had 31% higher FFA (P = 0.0002) and 20% higher triglycerides (P = 0.025) than non-carriers. The same haplotype was associated with increased **risk** of CAD in 197 type 2 diabetic individuals from the US (OR = 2.3, 95% CI 1.2-4.2). A similar tendency was observed in a group of 321 type 2 diabetic individuals from Italy (OR = 1.4, 0.9-2.3), resulting in an overall **relative risk** of 1.6 (1.1-2.3, P = 0.015) in the two populations considered together. By targeted resequencing, we identified a common variant in the CD36 promoter that is in strong LD with the AGGIG haplotype and could be partly responsible for these findings. In conclusion, this comprehensive study of CD36 variability indicates that the common polymorphisms at this locus modulate lipid metabolism and **cardiovascular risk** in Caucasians.

L2 ANSWER 37 OF 80 MEDLINE on STN
Full Text
AN 2004311821 MEDLINE
DN PubMed ID: 15213208
TI Estrogen receptor alpha gene polymorphisms and **risk** of myocardial infarction.
AU Schuit Stephanie C E; Oei Hok-Hay S; Witteman Jacqueline C M; Geurts van Kessel Corine H; van Meurs Joyce B J; Nijhuis Rogier L; van Leeuwen Johannes P T M; de Jong Frank H; Zillikens M Carola; Hofman Albert; Pols Huibert A P; Uitterlinden Andre G
CS Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands.
SO JAMA : the journal of the American Medical Association, (2004 Jun 23) Vol. 291, No. 24, pp. 2969-77.
Journal code: 7501160. E-ISSN: 1538-3598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200406
ED Entered STN: 25 Jun 2004
Last Updated on STN: 29 Jun 2004
Entered Medline: 28 Jun 2004
AB CONTEXT: The role of estrogens in ischemic heart disease (IHD) is uncertain. Evidence suggests that genetic variations in the estrogen receptor alpha (ESR1) gene may influence IHD **risk**, but the role of common sequence variations in the ESR1 gene is unclear. OBJECTIVE: To determine whether the ESR1 haplotype created by the c.454-397T>C (PvuII) and c.454-351A>G (XbaI) polymorphisms is associated with myocardial infarction (MI) and IHD **risk**. DESIGN, SETTING, AND PARTICIPANTS: In 2617 men and 3791 postmenopausal women from The Rotterdam Study (enrollment between 1989-1993 and follow-up to January 2000), a population-based, prospective cohort study of participants aged 55 years and older, ESR1 c.454-397T>C and c.454-351A>G haplotypes were determined. Detailed interviews and physical examinations were performed, blood samples were obtained, and **cardiovascular risk** factors were assessed. MAIN OUTCOME MEASURE: The primary outcome was MI and IHD defined as MIs, revascularization procedures, and IHD mortality. RESULTS: Approximately

29% of women and 28.2% of men were homozygous carriers of the ESR1 haplotype 1 (-397 T and -351 A) allele, 49% of women and 50% of men were heterozygous carriers, and 22% of women and 21.4% of men were noncarriers. During a mean follow-up of 7.0 years, 285 participants (115 women; 170 men) had MI, and 440 (168 women; 272 men) had an IHD event, of which 97 were fatal. After adjustment for known **cardiovascular risk** factors, female heterozygous carriers of haplotype 1 had an increased **risk** of MI (event rate, 2.8%; **relative risk** [RR], 2.23; 95% confidence interval [CI], 1.13-4.43) compared with noncarriers (event rate, 1.3%), whereas homozygous carriers had an increased **risk** (event rate, 3.2%; RR, 2.48; 95% CI, 1.22-5.03). For IHD events, we observed a similar association. In women, the effect of haplotype 1 on fatal IHD was larger than on nonfatal IHD. In men, the ESR1 haplotypes were not associated with an increased **risk** of MI (event rate, 5.7%; RR, 0.93; 95% CI, 0.59-1.46 for heterozygous carriers; and event rate, 5.1%; RR, 0.82; 95% CI, 0.49-1.38 for homozygous carriers) compared with noncarriers (event rate, 5.8%) and were not associated with an increased **risk** of IHD. CONCLUSIONS: In this population-based, prospective cohort study, postmenopausal women who carry ESR1 haplotype 1 (c.454-397 T allele and c.454-351 A allele) have an increased **risk** of MI and IHD, independent of known **cardiovascular risk** factors. In men, no association was observed.

L2 ANSWER 38 OF 80 MEDLINE on STN
Full Text
AN 2004307800 MEDLINE
DN PubMed ID: 15211444
TI Association between ENOS gene polymorphism and **cardiovascular** events in nondiabetic hemodialysis patients: a prospective study.
AU Asakimori Yukiteru; Yorioka Noriaki; Tanaka Junko; Takasugi Norihisa; Harada Satoru; Shigemoto Kenichiro; Yamashita Kazuomi; Usui Koji; Arita Michiko; Kohno Nobuoki
CS Department of Molecular and Internal Medicine , Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan.
SO American journal of kidney diseases : the official journal of the National Kidney Foundation, (2004 Jul) Vol. 44, No. 1, pp. 112-20.
Journal code: 8110075. E-ISSN: 1523-6838.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200410
ED Entered STN: 24 Jun 2004
Last Updated on STN: 27 Oct 2004
Entered Medline: 26 Oct 2004
AB BACKGROUND: Synthesis of nitric oxide by endothelial nitric oxide synthase (ENOS) plays a key role in the atherosclerotic process. Several polymorphisms of the gene encoding ENOS are now known and have been investigated with respect to their influence on **cardiovascular** disease **risk** in the general population. The authors prospectively investigated whether ENOS gene polymorphisms determined the **risk** of **cardiovascular** complications in a cohort of hemodialysis patients. METHODS: A total of 335 nondiabetic hemodialysis patients were **genotyped** for 3 ENOS polymorphisms (T-786-->C, intron 4, and Glu298Asp polymorphism) and were followed up prospectively for a mean of 44.2 +/- 9.0 months. The end-points of the study were major cardiac, cerebrovascular, or peripheral vascular events. RESULTS: Two ENOS polymorphisms were associated with **cardiovascular** events: a T to C substitution at position -786 of the promoter and a deletion-insertion in intron 4 (the a allele having 4 repeats of a consensus sequence and the b allele having 5 repeats). A total of 84 subjects were -786C carriers (CC+TC), and 15 (18%) suffered from **cardiovascular** events compared with only 13 of 251 TT patients (5%). The **relative risk** of **cardiovascular** events was higher for -786C carriers compared with noncarriers (**relative risk**: 2.05, P = 0.0003). It was also higher for a allele carriers (intron 4 polymorphism) compared with noncarriers (**relative risk**: 1.97, P = 0.0005). CONCLUSION: T-786-->C polymorphism and intron 4 polymorphism, but not Glu298Asp polymorphism, of the ENOS gene can influence the **risk** of **cardiovascular** events in Japanese nondiabetic hemodialysis patients.

L2 ANSWER 39 OF 80 MEDLINE on STN
Full Text
AN 2003612495 MEDLINE

DN PubMed ID: 14695540
TI Detection of thirty novel FBN1 mutations in patients with Marfan syndrome or a related fibrillinopathy.
AU Biggin Andrew; Holman Katherine; Brett Maggie; Bennetts Bruce; Ades Lesley
CS Marfan Research Group, The Children's Hospital at Westmead, NSW, Australia.
SO Human mutation, (2004 Jan) Vol. 23, No. 1, pp. 99.
Journal code: 9215429. E-ISSN: 1098-1004.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200403
ED Entered STN: 30 Dec 2003
Last Updated on STN: 10 Mar 2004
Entered Medline: 9 Mar 2004
AB Marfan syndrome (MFS) is a disorder of the extracellular matrix caused by mutations in the gene encoding fibrillin-1 (FBN1). Recent studies have illustrated the variability in disease severity and clinical manifestations of MFS. Useful **genotype**-phenotype correlations have been slow to emerge. We screened 57 unrelated patients with MFS or a Marfan-like phenotype using a combination of SSCP and/or DHPLC. We detected 49 different FBN1 mutations, 30 (62%) of which were novel. The mutations comprised 38 substitutions (78%), 10 deletions (20%), and one duplication (2%). There were 28 missense (57%), nine frameshift (18%), eight splice site (16%), and four nonsense mutations (8 %). **Genotype**-phenotype analysis revealed that patients with an identified FBN1 mutation were more likely to have ectopia lentis and **cardiovascular** complications compared to those without an identifiable mutation (**relative risks** of 4.6 and 1.9, respectively). Ectopia lentis was also found to be more prevalent in patients whose mutations involved a cysteine substitution (**relative risk** 1.6) and less prevalent in those with premature termination mutations (**relative risk** 0.4). In our hands, we achieved 93% mutation detection for DHPLC analysis of patients who fulfilled the Ghent criteria. Further analysis of detailed clinical information and mutation data may help to anticipate the clinical consequences of specific FBN1 mutations.

L2 ANSWER 40 OF 80 MEDLINE on STN
Full Text
AN 2003578529 MEDLINE
DN PubMed ID: 14660992
TI The cholesteryl ester transfer protein Taq1B gene polymorphism predicts clinical benefit of statin therapy in patients with significant coronary artery disease.
AU Carlquist John F; Muhlestein Joseph B; Horne Benjamin D; Hart Noal I; Bair Tami L; Molhuizen Henri O F; Anderson Jeffrey L
CS Cardiovascular Department, LDS Hospital, Salt Lake City, Utah 84143, USA.. ldjcarlq@ihc.com
SO American heart journal, (2003 Dec) Vol. 146, No. 6, pp. 1007-14.
Journal code: 0370465. E-ISSN: 1097-6744.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200401
ED Entered STN: 16 Dec 2003
Last Updated on STN: 14 Jan 2004
Entered Medline: 13 Jan 2004
AB BACKGROUND: Cholesteryl ester transfer protein (CETP) regulates plasma lipid distribution. A polymorphism in the CETP gene (Taq1B) is associated with CETP activity, HDL concentration, atherosclerosis progression, and response to statins, and may influence **cardiovascular** (CV) events. We studied CETP Taq1B **genotype**, plasma HDL, and clinical events among all patients and patients stratified by statin treatment. METHODS: Consenting patients (n = 2531) with significant coronary artery disease (> or =1 lesion of > or =70% stenosis) undergoing coronary arteriography were **genotyped**, grouped by statin prescription at hospital discharge, and prospectively followed-up for the outcomes of all-cause mortality and

myocardial infarction. RESULTS: CETP Taq1B **genotype** frequencies were: B1B1, 32.9%; B1B2, 50.3%; and B2B2 16.8%. Plasma HDL was reduced for B1B1 patients (33 +/- 12 mg/dL, vs 36 +/- 13 mg/dL and 36 +/- 13 mg/dL for B1B2 and B2B2, respectively, P for trend =.003). Overall, event rates did not differ between **genotypes**. Event rates were similar among untreated (24.8%) and statin-treated (24.2%) B1 homozygotes (P = NS); statins significantly reduced events for B1B2 subjects (28.0% vs 21.0%, P =.009) and for B2B2 subjects (26.4% vs 17.4%, P =.048). Therapeutic benefit for B2 carriers remained after adjustment for covariates, and regression interaction analysis showed that B2 carriers experienced reduced events (**relative risk** [RR] 0.62, 95% CI 0.45-0.86), but statins did not benefit those with B1B1 (RR 1.09, 95% CI 0.70-1.7; P for interaction =.02). Findings were similar for the end point of death alone, although a modest benefit was seen in B1B1 patients (RR 0.67, P =.10), in addition to the strong benefit for B1B2 (RR 0.53, P =.001) and B2B2 (RR 0.28, P =.001). CONCLUSIONS: The CETP Taq1B polymorphism is associated with differential HDL levels but no significant differential in CV **risk** in the absence of treatment. Importantly, however, CV event reduction by statin therapy is substantially enhanced in the presence of a B2 allele. Our findings suggest, for the first time, the potential of CETP Taq1B **genotyping** to enable more effective, pharmacogenetically directed therapy.

L2 ANSWER 41 OF 80 MEDLINE on STN
Full Text
AN 2003577694 MEDLINE
DN PubMed ID: 14605330
TI 4G/4G **genotype** of PAI-1 gene is associated with reduced **risk** of stroke in elderly.
AU Hoekstra Tiny; Geleijnse Johanna M; Kluft Cornelis; Giltay Erik J; Kok Frans J; Schouten Evert G
CS Division of Human Nutrition, Wageningen University, Netherlands.
SO Stroke; a journal of cerebral circulation, (2003 Dec) Vol. 34, No. 12, pp. 2822-8. Electronic Publication: 2003-11-06.
Journal code: 0235266. E-ISSN: 1524-4628.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 16 Dec 2003
Last Updated on STN: 6 Jan 2004
Entered Medline: 5 Jan 2004
AB BACKGROUND AND PURPOSE: Plasminogen activator inhibitor type 1 (PAI-1) is the main inhibitor of fibrinolysis, and high levels may increase the **risk** of **cardiovascular** disease. The 4G/5G polymorphism affects PAI-1 gene transcription with lower levels of plasma PAI-1 in the presence of the 5G allele. We investigated whether plasma PAI-1 and 4G/5G **genotype** would predict the occurrence of **cardiovascular** events at old age. METHODS: **Relative risks** for **cardiovascular** events and all-cause mortality were obtained in strata of PAI-1 activity and 4G/5G **genotype** in a population-based study of 637 Dutch elderly with 7.8 years of follow-up. RESULTS: The 4G/4G **genotype** was associated with a decreased **risk** of stroke (**relative risk** [RR]=0.4; 95% CI, 0.2 to 0.9), transient ischemic attack (RR=0.3; 95% CI, 0.1 to 0.8), and **cardiovascular** mortality (RR=0.5; 95% CI, 0.3 to 1.0) after adjustment for age, sex, and time of blood sampling. 4G carriers had an increased **risk** of myocardial infarction, but this was not statistically significant. Subjects with high plasma PAI-1 activity were at increased **risk** of stroke (RR=3.3 in highest versus lowest tertile; 95% CI, 1.5 to 7.1), **cardiovascular** mortality (RR=2.3; 95% CI, 1.2 to 4.4), and all-cause mortality (RR=1.5; 95% CI, 1.1 to 2.1). CONCLUSIONS: Our results provide support for a protective effect of the 4G allele against stroke, which is notable given the direct relationship between stroke and PAI-1 activity. We hypothesize that a local increase in tissue PAI-1 associated with the 4G allele may stabilize plaques, thereby reducing the **risk** of cerebrovascular disease.

L2 ANSWER 42 OF 80 MEDLINE on STN
Full Text
AN 2003553997 MEDLINE
DN PubMed ID: 14635166

TI Consistency of genetic analyses in longitudinal data: observations from the GAW13 Framingham Heart Study data.
AU Diego Vincent P; Atwood Larry; Mathias Rasika A; Almasy Laura
CS Department of Genetics, Southwest Foundation for Biomedical Research, San Antonio, Texas 78245, USA.
NC GM31575 (United States NIGMS)
MH59490 (United States NIMH)
SO Genetic epidemiology, (2003) Vol. 25 Suppl 1, pp. S29-35.
Journal code: 8411723. ISSN: 0741-0395.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200409
ED Entered STN: 25 Nov 2003
Last Updated on STN: 25 Sep 2004
Entered Medline: 24 Sep 2004
AB This paper examines the consistency of genetic analyses across time, both in the context of replicating results from one data collection point to the next, and from the perspective of modeling longitudinal processes. This summary originates from the examination of findings from nine papers from Genetic Analysis Workshop (GAW) 13 that reported on analyses of longitudinal data of a variety of traits from the Framingham Heart Study. These analyses include both assessments of consistency of aggregate genetic effects, in the form of estimation of heritability and **relative risk** of disease, as well as localization of quantitative trait loci (QTLs) by genome-wide linkage screens. Consistency varied widely by trait, possibly reflecting differences in measurement error, secular trends, or underlying biological features such as **genotype** x age interaction. Quantitatively, comparing magnitudes of estimates across age or time, heritability estimates showed greater consistency than LOD scores. However, qualitatively, the same regions of interest were often identified in genome scans from different time points or different ages. Estimates of sibling recurrence **risk**, on the other hand, showed little consistency. Heritabilities were greater when participants were matched by age than when they were matched by date of examination. Multivariate approaches, either in use of multiple traits or in use of multiple measures of the same trait, appeared to provide stronger genetic signals both for **relative risk** and for linkage. Finally, modeling of longitudinal processes provided evidence for **genotype** x age interactions that may partially explain variation in results of genetic analyses across time or age.

L2 ANSWER 43 OF 80 MEDLINE on STN
Full Text
AN 2003508489 MEDLINE
DN PubMed ID: 14584430
TI [Molecular genetic aspects of arrhythmias].
Molekularne geneticke aspekty v arytmologii.
AU Novotny T
CS Interni kardiologicka klinika Lekarske fakulty MU a FN Brno.
SO Vnitr ni lekar stvi, (2003 Sep) Vol. 49, No. 9, pp. 768-72.
Journal code: 0413602. ISSN: 0042-773X.
CY Czech Republic
DT (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA Czech
FS Priority Journals
EM 200312
ED Entered STN: 31 Oct 2003
Last Updated on STN: 19 Dec 2003
Entered Medline: 4 Dec 2003
AB The sequencing of human genome was completed in 2001. The position of particular DNA base is established-i.e. we know all "letters" in the "book" but we understand only limited number of "words" i. e. only limited number of genes was identified. And the human genome consists of about 30,000 genes from which through the mechanism of alternative RNA splicing more than 100,000 genes can be derived. All the genes of one individual form the **genotype**. The expression of **genotype** in particular

environment forms the phenotype. What is not present in **genotype** can neither be present in phenotype. In the last decade a substantial progress was achieved in understanding of membrane processes mostly due to research of relatively rare inherited monogenous arrhythmic syndromes--first of all the long QT syndrome. It is caused by mutations in ion channel genes and it provides a model of arrhythmogenesis on molecular level. Ventricular arrhythmias are important cause of mortality in patients with **cardiovascular** diseases. New studies have provided strong evidence for familial sudden cardiac death (SCD) aggregation and therefore also genetic influence. Parental history of SCD increases the **relative risk** of SCD for offspring to 1.8. In the case of both maternal and paternal SCD events the **risk** for offspring is a remarkable 9.4. There are 3 pathways by which genetic variation may contribute to **risk** for SCD: 1. alterations in electrogenesis and conduction, 2. formation and stability of atherosclerotic plaque, thrombogenesis and ischemia within the coronary circulation, 3. control of myocardial excitability and vascular motorics. The main objective of both today and future research is identification of inheritable "molecular" **risk** factors of arrhythmias. Understanding of this level of pathophysiological processes will subsequently lead to new generation of both diagnostic and therapeutic methods.

L2 ANSWER 44 OF 80 MEDLINE on STN
Full Text
AN 2003454185 MEDLINE
DN PubMed ID: 14514737
TI Role of the endothelin-1 gene locus for renal impairment in the general nondiabetic population.
AU Pinto-Sietsma Sara-Joan; Herrmann Stefan-Martin; Schmidt-Petersen Klaus; Niu Tianhua; Hillege Hans L; Janssen Wilbert M T; de Zeeuw Dick; de Jong Paul; Kreutz Reinhold
CS Department of Internal Medicine, Division of Nephrology, Academic Hospital Groningen, University Groningen, Groningen, The Netherlands.
SO Journal of the American Society of Nephrology : JASN, (2003 Oct) Vol. 14, No. 10, pp. 2596-602.
Journal code: 9013836. ISSN: 1046-6673.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200409
ED Entered STN: 30 Sep 2003
Last Updated on STN: 15 Sep 2004
Entered Medline: 14 Sep 2004
AB A decreased GFR in the range of mild renal insufficiency and an increased urinary albumin excretion (UAE) rate in the range of microalbuminuria are important **cardiovascular risk** factors. Endothelin-1 (ET-1) has been suggested to be a major disease promoting factor in renal disease. The role of the ET-1 gene locus (EDN1) for renal function in the general nondiabetic population was evaluated. To explore the overall relevance of EDN1, two suitable single-nucleotide polymorphisms, EDN1 K198N and EDN1 T-1370G, were selected, and haplotype analysis was performed. Determined were **genotypes** in 7291 nondiabetic subjects from the Prevention of Renal and Vascular End-Stage Disease (PREVEND) study. Genetic analysis was related to UAE and GFR as continuous variables and to microalbuminuria and diminished filtration as dichotomous traits. In a logistic regression analysis, no significant higher **risk** for increased UAE, microalbuminuria, decreased GFR, or diminished filtration could be observed for either single-nucleotide polymorphism separately. Haplotype analysis revealed that individuals with the homozygous G-N haplotype (compound EDN1 -1370GG/198NN **genotype**) have a lower GFR than the remaining subjects ($P < 0.05$) and exhibit a significant higher **risk** for the presence of a diminished filtration (**relative risk**, 2.4; 95% confidence interval, 1.07 to 5.33; $P < 0.05$). Further analysis demonstrated no association between this haplotype and UAE or plasma ET-1 levels. Although a functional relevance of the EDN1 G-N haplotype itself remains unclear, the data demonstrate that genetic variation at the EDN1 locus has a significant effect on glomerular filtration but not on UAE in the general nondiabetic population.

L2 ANSWER 45 OF 80 MEDLINE on STN

Full Text
AN 2003399687 MEDLINE
DN PubMed ID: 12932598
TI Platelet glycoprotein IIb/IIIa Pl(A2)/Pl(A2) homozygosity associated with **risk** of ischemic **cardiovascular** disease and myocardial infarction in young men: the Copenhagen City Heart Study.
AU Bojesen Stig E; Juul Klaus; Schnohr Peter; Tybjaerg-Hansen Anne; Nordestgaard Borge G
CS Department of Clinical Biochemistry, Herlev University Hospital, Herlev, Denmark. (Copenhagen City Heart Study).
SO Journal of the American College of Cardiology, (2003 Aug 20) Vol. 42, No. 4, pp. 661-7.
Journal code: 8301365. ISSN: 0735-1097.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200309
ED Entered STN: 27 Aug 2003
Last Updated on STN: 1 Oct 2003
Entered Medline: 30 Sep 2003
AB OBJECTIVES: We tested the hypothesis that platelet glycoprotein (GP) IIb/IIIa Pl(A2)/Pl(A2) homozygotes or Pl(A1)/Pl(A2) heterozygotes versus Pl(A1)/Pl(A1) noncarriers have increased **risk** of ischemic **cardiovascular** disease and myocardial infarction (MI), stratified for age and gender. BACKGROUND: The GP IIb/IIIa Pl(A1)/Pl(A2) polymorphism influences aggregation of platelets; however, an association between ischemic **cardiovascular** disease and heterozygosity remains controversial, and association with homozygosity is largely unexplored. METHODS: We **genotyped** the participants of the Copenhagen City Heart Study, a prospective **cardiovascular** investigation of the Danish general population (n = 9,149, 22-year follow-up) and assessed the **risk** of ischemic **cardiovascular** disease in heterozygotes or homozygotes versus noncarriers. RESULTS: Of the participants, 70.0%, 27.3%, and 2.7% were noncarriers, heterozygotes, or homozygotes, respectively. Incidence of ischemic **cardiovascular** disease was 167 and 103 per 10,000 person-years in homozygous and noncarrier men (log-rank: p = 0.006), whereas this difference was not observed in women (p = 0.33) (**genotype**.gender interaction: p = 0.03). In homozygous versus noncarrier men <40 years of age, 40 to 50 years, and >50 years at entry, age-adjusted **relative risks** (RRs) of ischemic **cardiovascular** disease were 3.6 (1.4 to 9.0), 2.4 (1.3 to 4.6), and 1.0 (0.6 to 1.8), respectively (age.**genotype** interaction in men: p = 0.04); equivalent multifactorially adjusted RRs were 3.0 (1.1 to 8.0), 2.0 (1.0 to 3.9), and 1.0 (0.6 to 1.8), respectively. The corresponding age-adjusted RR values of MI in men were 5.2 (1.5 to 18), 3.5 (1.6 to 7.5), and 0.5 (0.1 to 1.5), respectively (age.**genotype** interaction in men: p = 0.002); equivalent multifactorially adjusted RRs were 3.8 (1.0 to 15), 3.1 (1.4 to 6.9), and 0.5 (0.2 to 1.5), respectively. CONCLUSIONS: Pl(A2)/Pl(A2) homozygosity is associated with a three-fold and four-fold **risk** of ischemic **cardiovascular** disease and MI in young men.

L2 ANSWER 46 OF 80 MEDLINE on STN
Full Text
AN 2003288410 MEDLINE
DN PubMed ID: 12767551
TI Association of two angiotensinogen gene polymorphisms, M235T and G(-6)A, with chronic heart failure.
AU Goldbergova Monika; Spinarova Lenka; Spinar Jindrich; Toman Jiri; Vasku Anna; Vacha Jiri
CS lnstitute of Pathological Physiology, Faculty of Medicine, Masaryk University Brno, Komenskeho nam.2, 662 43, Brno, Czech Republic. goldberg@med.muni.cz. <goldberg@med.muni.cz>
SO International journal of cardiology, (2003 Jun) Vol. 89, No. 2-3, pp. 267-72.
Journal code: 8200291. ISSN: 0167-5273.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals

EM 200310
ED Entered STN: 21 Jun 2003
Last Updated on STN: 31 Oct 2003
Entered Medline: 30 Oct 2003
AB The aim of the study was to focus on the relationship between the angiotensinogen (AGT) gene polymorphisms, M235T and promoter G(-6)A, and chronic heart failure in the Czech population. A total of 158 patients with chronic heart failure (functional class NYHA II-IV, ejection fraction <40%, cardiothoracic index >50%) were compared with a control group of 200 subjects of similar age and sex distribution, without any personal history of **cardiovascular** diseases. The AGT gene polymorphisms were detected by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) methods. No significant differences in distributions of AGT **genotypes** between patients with chronic heart failure (CHF) and controls were found. The differences in distributions of alleles in AGT M235T (P(a)=0.02) and **genotypes** in AGT G(-6)A (P(g)=0.017) were found within women groups. Within CHF patients the distribution of AGT G(-6)A **genotypes** was not consistent with Hardy-Weinberg equilibrium (P=0.0001). We found significant **relative risk** of CHF in the GGMT **genotype**, OR=2.63 with 95% CI 1.39-4.95, P(corr)=0.01 (in the male group OR=1.83, 95% CI 0.92-3.66, P(corr)=0.3; in the female group OR=15.5, 95% CI 1.86-129.42, P(corr)=0.008). We provide evidence of increased **risk** in subjects with the GGMT variant of associated **genotype** of AGT gene for CHF, especially of fifteen-fold **risk** of this variant in women.

L2 ANSWER 47 OF 80 MEDLINE on STN
Full Text
AN 2003266097 MEDLINE
DN PubMed ID: 12790760
TI Office blood pressure, heart rate and A(-596)G interleukin-6 gene polymorphism in apparently healthy Czech middle-aged population.
AU Vasku A; Soucek M; Goldbergova M; Vacha J
CS Institute of Pathological Physiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic.. avasku@med.muni.cz
SO Physiological research / Academia Scientiarum Bohemoslovaca, (2003) Vol. 52, No. 3, pp. 291-7.
Journal code: 9112413. ISSN: 0862-8408.
CY Czech Republic
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 8 Jun 2003
Last Updated on STN: 23 Apr 2004
Entered Medline: 22 Apr 2004
AB The aim of the study was to assess the association between promoter polymorphism [A(-596)G] in interleukin-6 gene and office systolic and diastolic blood pressures, and the heart rate (HR) in apparently healthy Czech subjects. Furthermore, we evaluated the possible influence of gender, BMI and smoking on these supposed associations. An age-matched (40-50 years) and gender-matched (F/M=81/89) sample of apparently healthy Czech subjects (n=170, F/M=81/89) without hypertension, other **cardiovascular** diseases or diabetes was examined. The A(-596)G Il-6 gene polymorphism was detected by the PCR method. No differences in **genotype** distribution and/or allelic frequency was found between groups with lower systolic blood pressure (L 122 mm Hg) and higher systolic blood pressure (> 122 mm Hg). Similarly, no differences in the IL-6 polymorphism were found between lower (L 86 mm Hg) and higher (> 86 mm Hg) diastolic blood pressure groups. However, we proved a significant increase of **genotypes** AG+GG as well as the allele (-596)G in higher (>78 beats/min) heart rate group. The **genotypes** AG+GG represent significantly higher **relative risk** for higher HR frequency, especially in women. Among lean persons with a low heart rate frequency, fewer AG+GG **genotypes** were determined than among any other subjects. The **genotypes** AG+GG are more frequent in non-smoking persons with higher HR compared to non-smoking subjects with lower HR, especially in women. Gender, BMI and smoking substantially modify the distribution of A(-596)G Il-6 gene polymorphism in apparently healthy persons with lower or higher heart rate.

L2 ANSWER 48 OF 80 MEDLINE on STN

Full Text
AN 2003111571 MEDLINE
DN PubMed ID: 12624641
TI Association between TAFI antigen and Ala147Thr polymorphism of the TAFI gene and the angina pectoris incidence. The PRIME Study (Prospective Epidemiological Study of MI).
AU Morange Pierre E; Juhan-Vague Irene; Scarabin Pierre Y; Alessi Marie C; Luc Gerald; Arveiler Dominique; Ferrieres Jean; Amouyel Philippe; Evans Alun; Ducimetiere Pierre
CS Department of Hematology, Hospital de la Timone, INSERM 99-36 Marseilles, France. (PRIME Study group).
SO Thrombosis and haemostasis, (2003 Mar) Vol. 89, No. 3, pp. 554-60. Journal code: 7608063. ISSN: 0340-6245.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 8 Mar 2003
Last Updated on STN: 31 Oct 2003
Entered Medline: 30 Oct 2003
AB Thrombin activatable fibrinolysis inhibitor (TAFI), a recently described inhibitor of fibrinolysis, has been hypothesized as playing a role in atherothrombosis. However, the evidence from retrospective studies, which have evaluated the role of TAFI in vascular **risk**, is conflicting. In a prospective cohort (the PRIME Study) of nearly 10 000 apparently healthy men recruited in France (Lille, Strasbourg, Toulouse) and Northern Ireland (Belfast), we measured baseline plasma concentration of TAFI antigen among 143 participants (81 from France and 62 from Ireland) who subsequently developed angina pectoris and among 286 age-matched participants who remained free of disease during the 5 years of follow-up. **Genotyping** of the Ala147Thr polymorphism located in the TAFI gene was performed using an allele specific PCR. In France, mean levels of TAFI were significantly higher at baseline among men who subsequently developed angina pectoris compared with their control subjects (119 versus 107 %; p = 0.02). The **risk** of future angina pectoris increased with increasing tertiles of TAFI (p = 0.02), such that men in the highest tertile at study entry had a 5-fold higher **relative risk** than those in the lowest tertile (95% confidence interval, 1.38 to 18.58) after controlling for the conventional **cardiovascular risk** factors. No such difference was observed in Northern Ireland. In France, Thr/Thr carriers of the Ala147Thr polymorphism were significantly more frequent in cases than in controls (p = 0.01) leading to a **relative risk** of angina pectoris of 2.7 (95%CI 1.2-5.8). Increase in plasma TAFI antigen levels is a **risk** factor for angina pectoris in France. **Genotyping** for the Ala147Thr polymorphism seems to be a reliable tool to assess the **risk** mediated by TAFI.

L2 ANSWER 49 OF 80 MEDLINE on STN
Full Text
AN 2003069637 MEDLINE
DN PubMed ID: 12566975
TI Association between the G protein beta3 subunit 825t allele and radial artery hypertrophy.
AU Hanon Olivier; Luong Vu; Mourad Jean Jacques; Bortolotto Luiz A; Safar Michel; Girerd Xavier
CS Department of Internal Medicine and INSERM U337, Broussais Hospital, 96 rue Didot, F-75014 Paris, France.
SO Journal of vascular research, (2002 Nov-Dec) Vol. 39, No. 6, pp. 497-503. Journal code: 9206092. ISSN: 1018-1172.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 14 Feb 2003
Last Updated on STN: 7 Mar 2003
Entered Medline: 6 Mar 2003
AB The GNB3 C825T gene polymorphism has recently been identified and associated with hypertension, obesity and left ventricular hypertrophy. The aim of the study was to determine the relationship between the C825T

polymorphism of the gene encoding for the G protein beta3 subunit (GNB3 C825T) and vascular hypertrophy. We studied a cohort of 306 subjects (age 49 +/- 12 years) without evidence of **cardiovascular** disease and never treated with **cardiovascular** drugs. Vascular phenotypes were evaluated for the common carotid and radial arteries using high-resolution echo-tracking devices. **Genotype** frequencies were in agreement with the Hardy-Weinberg equilibrium. For the radial artery, mean wall thickness was significantly higher in subjects carrying the 825T allele than in CC **genotype** subjects (240 +/- 54 microm for CT **genotype** and 241 +/- 53 microm for TT **genotype** vs. 222 +/- 52 microm for CC **genotype**, p = 0.01). The frequency of the 825T allele was significantly different in subjects with (52%) and without (35%) radial artery hypertrophy (chi(2) = 10.88, p < 0.001). The **relative risk** of radial artery hypertrophy in subjects carrying the 825T allele compared with those with the CC **genotype** was 3.02 (95% CI 1.53- 5.95). A logistic regression analysis indicated that the positive and significant association between the 825T allele and radial artery hypertrophy was independent of age, blood pressure, gender and BMI. In contrast, no association between **genotypes** and carotid artery wall thickening was observed. These results suggest that some genetic characteristics determine in part the patterns of radial artery geometrical changes. As the 825T allele is associated with vascular hypertrophy of a muscular artery but not with structural changes of an elastic artery, we hypothesize that the 825T allele may be a genetic marker of arteriolosclerosis.

L2 ANSWER 50 OF 80 MEDLINE on STN
Full Text
AN 2002664889 MEDLINE
DN PubMed ID: 12425488
TI Angiotensin-converting enzyme (ACE) insertion/deletion polymorphism and survival in a cohort of chronic hemodialysis patients.
AU Higashiuesato Y; Tana T; Tozawa M; Iseki C; Iseki K; Fukiyama K; Takishita S
CS Third Department of Internal Medicine, University of the Ryukyus, Okinawa, Japan.. yhigashi-ryk@umin.ac.jp
SO Clinical nephrology, (2002 Nov) Vol. 58, No. 5, pp. 370-5.
Journal code: 0364441. ISSN: 0301-0430.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 12 Nov 2002
Last Updated on STN: 26 Feb 2003
Entered Medline: 25 Feb 2003
AB BACKGROUND: There are conflicting reports regarding the relationship between the angiotensin-converting enzyme (ACE) insertion/deletion (I/D) polymorphism and the initiation and progression of **cardiovascular** disease. Moreover, there is no report regarding the relationship between the ACE I/D polymorphism and the prognosis of chronic dialysis patients. METHODS: We examined the frequency of the ACE I/D polymorphism in 727 chronic hemodialysis patients in Okinawa, Japan, and observed the prognosis over 2 years in 407 men and 320 women with mean age (SD) of 55.5 (13.9) years with a mean duration of dialysis of 84.3 (66.6) months. RESULTS: **Genotype** frequencies were 42.1% for II, 43.2% for ID, and 14.7% for DD. The **relative risks** of death were examined by Cox-proportional hazards analysis after adjusting for age, sex, age at the start of dialysis, presence of diabetes mellitus and hypertension and total cholesterol and serum albumin levels. The adjusted hazard ratio (95% confidence interval) was 1.03 (0.38 - 2.85) for DD **genotype** and 1.50 (0.83 - 2.70) for DD+ID **genotype** when compared to II **genotype**. CONCLUSION: ACE I/D polymorphism appears to have no relation to the short-term prognosis in chronic hemodialysis patients.

L2 ANSWER 51 OF 80 MEDLINE on STN
Full Text
AN 2002411177 MEDLINE
DN PubMed ID: 12164877
TI Anti-inflammatory interleukin-10 **genotype** protects dialysis patients from **cardiovascular** events.
AU Girndt Matthias; Kaul Harald; Sester Urban; Ulrich Christof; Sester

Martina; Georg Thomas; Kohler Hans
CS Medical Department IV, University of Homburg/Saar, Kirrberger Strasse 1, D-66421 Homburg/Saar, Germany.
SO Kidney international, (2002 Sep) Vol. 62, No. 3, pp. 949-55.
Journal code: 0323470. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(CLINICAL TRIAL)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 8 Aug 2002
Last Updated on STN: 12 Feb 2003
Entered Medline: 11 Feb 2003
AB BACKGROUND: Inflammatory processes play an important role for the progression of atherosclerosis. This can be studied particularly well in patients with chronic renal failure who are on hemodialysis, as they show systemic inflammation due to uremia and dialysis while suffering from premature mortality secondary to rapidly progressing atherosclerosis. Interleukin (IL)-10 is a regulatory cytokine that limits inflammatory processes. The quantitative production of IL-10 is subject to genetic variation based on polymorphisms in the promoter of its gene. We tested the hypothesis that the IL-10 **genotype**, by influencing the capacity to compensate for dialysis-induced systemic inflammation, determines the **risk** for **cardiovascular** complications. METHODS: Three hundred chronic hemodialysis patients were **genotyped** for the polymorphic bases at positions -1082 and -819 of the IL-10 promoter sequence. They were prospectively followed for a mean of 20.2 +/- 7.3 months. End-points of the study were major events related to cardiac, cerebrovascular or peripheral artery disease. RESULTS: The -1082A* allele, which is associated with low production of the cytokine IL-10 and elevated markers of systemic inflammation such as C reactive protein, was predictive for a higher **cardiovascular** morbidity (**relative risk** for **cardiovascular** events 2.76, 95% confidence interval 1.31 to 4.17, P = 0.004) compared to the -1082G* **genotype**. CONCLUSION: The IL-10 **genotype** influences the **risk** for **cardiovascular** events in hemodialysis patients and allows the definition of a high **risk** group. The data provide further evidence for a causal role of systemic inflammation for progressive atherosclerosis in dialysis patients.

L2 ANSWER 52 OF 80 MEDLINE on STN
Full Text
AN 2002400011 MEDLINE
DN PubMed ID: 12149201
TI Genetic variability in the extracellular matrix as a determinant of **cardiovascular risk**: association of type III collagen COL3A1 polymorphisms with coronary artery disease.
AU Muckian Clare; Fitzgerald Anthony; O'Neill Anne; O'Byrne Anna; Fitzgerald Desmond J; Shields Denis C
CS Department of Clinical Pharmacology, Royal College of Surgeons in Ireland, Dublin.
SO Blood, (2002 Aug 15) Vol. 100, No. 4, pp. 1220-3.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200209
ED Entered STN: 1 Aug 2002
Last Updated on STN: 13 Sep 2002
Entered Medline: 12 Sep 2002
AB Although common genetic variants in platelet collagen receptors influence platelet activation and thrombosis, the impact of polymorphisms in collagen genes on **cardiovascular** disease is unknown. To evaluate this, we **genotyped** a highly polymorphic intronic tandem repeat of the COL3A1 gene, encoding collagen type III, alpha 1. This revealed 4 common alleles (COL3A1-1, -2, -3, and -4). The 2 populations studied were as follows:

(1) a cross-sectional study of 703 acute coronary syndrome (ACS) patients with myocardial infarction (MI) and unstable angina, and (2) a prospective study of 924 Caucasian patients from the OPUS (Orbofiban in Patients with Unstable coronary Syndromes)-TIMI-16 trial of the oral GPIIb/IIIa antagonist orbofiban. In addition, we studied 306 control subjects and 224 patients with stable angina. In the case-control population, COL3A1-4 carriers were protected against ACS (odds ratio [OR] = 0.57, 95% CI = 0.35-0.91, P =.02) and stable angina (OR = 0.35, 95% CI = 0.16-0.74, P =.006). In the OPUS population, allele 4 again appeared protective against composite end points (death, MI, stroke, recurrent ischemia, and urgent rehospitalization) (**relative risk** [RR] = 0.41, 95% CI = 0.17-1.00). There were significant interactions between COL3A1-1 and -3 variants and treatment. Allele COL3A1-3 was associated with an increased **risk** of the composite end point (RR = 1.65, 95% CI = 1.07-2.55) in patients randomized to orbofiban, but appeared protective in placebo patients (RR = 0.53, 95% CI = 0.28-0.98). We conclude that variants in the COL3A1 gene, the product of which is a vessel-wall protein and platelet ligand, modulate the **risk** of coronary artery disease and could also modulate the response to antithrombotic therapy. This is the first reported association between polymorphisms of extracellular matrix components and **cardiovascular risk**.

L2 ANSWER 53 OF 80 MEDLINE on STN
Full Text
AN 2002351271 MEDLINE
DN PubMed ID: 12070000
TI Factor V Leiden: The Copenhagen City Heart Study and 2 meta-analyses.
AU Juul Klaus; Tybjaerg-Hansen Anne; Steffensen Rolf; Kofoed Steen; Jensen Gorm; Nordestgaard Borge Gronne
CS Department of Clinical Biochemistry, Herlev University Hospital, Herlev, Denmark.
SO Blood, (2002 Jul 1) Vol. 100, No. 1, pp. 3-10.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(META-ANALYSIS)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200207
ED Entered STN: 4 Jul 2002
Last Updated on STN: 27 Jul 2002
Entered Medline: 26 Jul 2002
AB Factor V Leiden (FVL) is associated with venous thrombosis; however, an association between FVL and arterial thrombosis remains controversial. We investigated FVL as a **risk** factor for myocardial infarction (MI), ischemic stroke (IS), or non-MI ischemic heart disease (non-MI-IHD). The design was 3 case-control studies and 3 prospective studies with 21 years' follow-up. The setting was the general population in Copenhagen, Denmark. The participants for The Copenhagen City Heart Study were 20- to 95-year-old participants without **cardiovascular** disease (control population, n = 7907) or participants diagnosed with MI (n = 469), IS (n = 231), or non-MI-IHD (n = 365). In addition, 3 independent patient populations from Copenhagen University Hospital with MI (n = 493), IS (n = 231), or non-MI-IHD (n = 448) were included. We measured FVL **genotype**; major **cardiovascular risk** factors; and MI, IS, and non-MI-IHD incidence and prevalence. Prevalences of FVL heterozygotes and homozygotes in control subjects from the general population were 7.7% and 0.2%. Odds ratios and **relative risks** of MI in FVL carriers (heterozygotes + homozygotes) versus noncarriers were 1.24 (95% confidence interval [CI], 0.91-1.69) and 0.83 (0.58-1.20) in case-control and prospective studies, respectively. Corresponding **risks** for IS were 0.92 (95% CI, 0.56-1.53) and 0.68 (0.45-1.04), and for non-MI-IHD 1.01 (95% CI, 0.71-1.44) and 0.97 (0.66-1.42). Findings from The Copenhagen City Heart Study suggest that FVL is not associated with MI, IS, or non-MI-IHD.

L2 ANSWER 54 OF 80 MEDLINE on STN
Full Text
AN 2002156981 MEDLINE
DN PubMed ID: 11888533
TI A prospective study of TaqIB polymorphism in the gene coding for cholesteryl ester transfer protein and **risk** of myocardial infarction in

middle-aged men.
AU Liu Simin; Schmitz Christian; Stampfer Meir J; Sacks Frank; Hennekens Charles H; Lindpaintner Klaus; Ridker Paul M; Liu Simm
CS Division of Preventive Medicine, Department of Medicine, Center for Cardiovascular Disease Prevention, Brigham and Women's Hospital and Harvard Medical School, 900 Commonwealth Avenue East, Boston, MA 02215, USA.
NC CA34944 (United States NCI)
CA40360 (United States NCI)
HL-26490 (United States NHLBI)
HL34595 (United States NHLBI)
SO Atherosclerosis, (2002 Apr) Vol. 161, No. 2, pp. 469-74.
Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200205
ED Entered STN: 13 Mar 2002
Last Updated on STN: 25 Feb 2003
Entered Medline: 14 May 2002
AB BACKGROUND: Molecular variations in the gene coding for the cholesteryl ester transfer protein (CETP) such as the TaqIB polymorphism are associated with higher plasma high-density lipoprotein (HDL) concentration. However, whether this polymorphism is associated with **risk** of myocardial infarction (MI) is uncertain. METHODS AND RESULTS: In a prospective cohort of 14916 apparently healthy men enrolled in the Physicians' Health Study, allelic status for the TaqIB polymorphism in the CETP gene was determined among 384 participants who subsequently developed a first MI (cases) and among an equal number of age and smoking-matched participants who remained free of **cardiovascular** disease during follow-up (controls). Overall, the B2B2 **genotype** was present in 17% of the study participants and was associated with higher HDL cholesterol levels (mean mg/dl [+/- S.D.], 45 +/- 11 for the B1B1 **genotype**, 48 +/- 13 for the B1B2 **genotype** and 50 +/- 12 for the B2B2 **genotype**; P=0.01). However, the **risk** of developing MI did not differ significantly across these three **genotypes**. After adjustment for coronary **risk** factors (but not HDL), the **relative risks** for future MI were 1.12(95% CI 0.74-1.70) for the B1B2 **genotype** and 0.95(95% CI 0.54-1.66) for the B2B2 **genotype**, compared with the B1B1 **genotype**. In subgroup analysis of individuals with low HDL levels, B2B2 **genotype** appeared to have a lower **risk** of MI compared with the B1B1 **genotype**. However, participants with high HDL were at lower **risk** of developing MI regardless of their CETP **genotype**. CONCLUSIONS: In this prospective study of apparently healthy middle-aged US men, carriers of the B2 allele of the TaqIB in the CETP gene had higher HDL concentrations, but did not have lower **risk** of MI. CONDENSED ABSTRACT: In a cohort of apparently healthy middle-aged US men, the relation between CETP **genotype** and MI **risk** was prospectively examined in a nested case-control study. After adjusting for coronary **risk** factors (but not HDL), the 9-year **risk** of developing MI did not differ significantly by **genotype**. Comparing to the B1B1 **genotype**, the **relative risks** for future MI were 1.12 (95% CI 0.74-1.70) for the B1B2 **genotype** and 0.95 (95% CI 0.54-1.66) for the B2B2 **genotype**.

L2 ANSWER 55 OF 80 MEDLINE on STN
Full Text
AN 2002059771 MEDLINE
DN PubMed ID: 11786115
TI Low TGF-beta1 serum levels are a **risk** factor for atherosclerosis disease in ESRD patients.
AU Stefoni Sergio; Cianciolo Giuseppe; Donati Gabriele; Dormi Ada; Silvestri Maria Grazia; Coli Luigi; De Pascalis Antonio; Iannelli Sandra
CS Nephrology Dialysis and Renal Transplantation Unit, Department of Clinical Medicine and Applied Biotechnology, S. Orsola University Hospital, Bologna, Italy.. sstefoni@almans.unibo.it
SO Kidney international, (2002 Jan) Vol. 61, No. 1, pp. 324-35.
Journal code: 0323470. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English

FS Priority Journals
EM 200203
ED Entered STN: 25 Jan 2002
Last Updated on STN: 7 Mar 2002
Entered Medline: 5 Mar 2002
AB BACKGROUND: It is thought that transforming growth factor-beta1 (TGF-beta1) might be a key inhibitor of atherogenesis in non-uremic patients. We evaluated the intra- and post-dialytic serum levels of TGF-beta1 in uremic patients to assess if TGF-beta1 is an independent **risk** factor for **cardiovascular** diseases, and if any correlation exists between TGF-beta1 and any yet known atherosclerotic **risk** factors. METHODS: We studied 155 patients who were on regular hemodialysis, with or without clinically significant atherosclerotic vascular disease. Forty-one apparently healthy people were enrolled as a control group. TGF-beta1 was evaluated during the midweek dialysis session, at times 0, 30, and 120 minues, at the end of the session, and 3 hours after the session's end. All hitherto known atherosclerotic **risk** factors also were evaluated. The investigation was performed over a 24-month follow-up. RESULTS: TGF-beta1 values (mean +/- SD) in dialysis patients were 26.64 +/- 7.0 ng/mL (N=155) compared with 42.31 +/- 6.0 ng/mL in the control group (N=41, P < 0.0001). A weak inverse correlation emerged between TGF-beta1 and age (r=-0.28), TGF-beta1 and lipoprotein(a) [Lp(a); r=-0.35], TGF-beta1 and C-reactive protein (CRP; r=-0.27), and TGF-beta1 and plasminogen activator inhibitor-1 (PAI-1; r=-0.41). TGF-beta1 also correlated with albumin (r=0.31). In the coronary heart disease (CHD) group (N=32) the TGF-beta1 was 26.2 +/- 4.9 ng/mL; in the cerebrovascular disease (**CVD**) group (N=8) it was 26.7 +/- 3.7 ng/mL and in the peripheral vascular disease (PVD) group (N=9) it was 25.4 +/- 1.7 ng/mL. In dialysis patients with no **cardiovascular** disease (N=80) TGF-beta1 was 35.1 +/- 6.8 ng/mL (P < 0.0001 vs. CHD, **CVD** and PVD patients). TGF-beta1 was significantly lower among those patients with triple coronary vessel disease than with the other CHD patients. The Cox analysis demonstrated that a 1 ng/mL reduction in TGF-beta1 concentration was associated with a 9% increase in the **relative risk** of a **cardiovascular** event. CONCLUSIONS: TGF-beta1 was significantly reduced in hemodialysis patients, in particular in those with severe **cardiovascular** disease. Baseline TGF-beta1, diabetes mellitus and serum albumin levels proved to be the only independent contributors to atherosclerotic **risk** in dialysis patients.

L2 ANSWER 56 OF 80 MEDLINE on STN
Full Text
AN 2002044894 MEDLINE
DN PubMed ID: 11755935
TI The T allele of the missense Glu(298)Asp endothelial nitric oxide synthase gene polymorphism is associated with coronary heart disease in younger individuals with high atherosclerotic **risk** profile.
AU Gardemann Andreas; Lohre Jana; Cayci Sevim; Katz Norbert; Tillmanns Harald; Haberbosch Werner
CS Institut fur Klinische Chemie und Pathobiochemie, Klinikum der Justus-Liebig-Universitat Giessen, Gaffky-Strasse 11, 35392 Giessen, Germany.. andreas.gardemann@klinchemie.med.uni-de
SO Atherosclerosis, (2002 Jan) Vol. 160, No. 1, pp. 167-75.
Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 24 Jan 2002
Last Updated on STN: 6 Apr 2002
Entered Medline: 5 Apr 2002
AB AIMS: Nitric oxide (NO) plays a protective role during atherogenesis. In the endothelium, NO is synthesised by the constitutive NO synthase (ecNOS). We analysed the relation of the ecNOS Glu(298)Asp and 4a/b gene polymorphisms to coronary artery disease (CAD) and myocardial infarction (MI) in a population of 3250 German subjects (533 healthy controls and 2717 individuals who underwent coronary angiography). RESULTS: Although in the total sample, the ecNOS T allele was not associated with the **risk** of CAD (P=0.054) and the extent of this disease (P=0.078), a restriction to younger individuals (age</=61, mean age) revealed an association of the

ecNOS T allele with an increased **risk** of CAD (1.43, 1.05-1.96; P=0.025) and with the severity of this disease (P=0.037). Similar observations were made in various high-**risk** populations. These associations were even more pronounced when the high-**risk** subgroups were restricted to younger individuals. For example, an odds ratio of 7.66 for CAD (95% CI, 2.0-29; P=0.003) was detected in diabetic individuals who were younger than 61 years. Also with respect to MI, the most pronounced associations of the ecNOS T allele with the **risk** of this disease were detected in younger individuals with at least one other **cardiovascular risk** factor. For example, in diabetics younger than 61 years, the **relative risk** for ecNOS T allele carriers was 9.73 (95% CI, 1.8-53; P=0.008). In contrast, the allele frequencies of the ecNOS 4a/b gene variation were essentially the same in controls and in CAD and MI patients. CONCLUSION: The present data extends earlier observations by the findings that predominantly younger T allele carriers of the ecNOS Glu(298)Asp gene polymorphism with various coronary high-**risk** profiles had an increased **risk** to suffer CAD and/or MI. In contrast, no evidence was found for an association of the ecNOS 4a/b gene polymorphism with coronary heart disease.

L2 ANSWER 57 OF 80 MEDLINE on STN
Full Text
AN 2001682511 MEDLINE
DN PubMed ID: 11728146
TI Mutation in the promoter region of the beta-fibrinogen gene and the **risk** of future myocardial infarction, stroke and venous thrombosis.
AU Blake G J; Schmitz C; Lindpaintner K; Ridker P M
CS The Center for Cardiovascular Disease Prevention, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02215, USA.
NC HL58755 (United States NHLBI)
SO European heart journal, (2001 Dec) Vol. 22, No. 24, pp. 2262-6. Journal code: 8006263. ISSN: 0195-668X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 3 Dec 2001
Last Updated on STN: 15 Feb 2002
Entered Medline: 14 Feb 2002
AB AIM: Polymorphisms in the promoter region of the beta-fibrinogen gene are associated with increased plasma fibrinogen levels. We investigated whether the distribution of the C148T polymorphism is associated with an increase in **cardiovascular risk**. METHODS AND RESULTS: In a nested case-control design, the distribution of the C148T polymorphism was investigated among 751 participants in the Physicians' Health Study who subsequently developed myocardial infarction, stroke or venous thromboembolism (cases) and among 751 age- and smoking-matched controls over follow-up of 8.6 years. Frequency of the T allele was similar among men who had myocardial infarction (22.7%, P=0.5), stroke (18.4%, P=0.2) or venous thromboembolism (17.0%, P=0.1) compared with those with no **cardiovascular** events (21.5%). The **relative risk** for any vascular event among men homozygous or heterozygous for the T allele compared with men homozygous for the C allele was 0.94 (95% CI 0.76-1.16). We found no evidence of an association between the T allele and myocardial infarction (**relative risk** 1.06; 95% CI 0.82-1.36), stroke (0.87, 0.63-1.21) or venous thromboembolism (0.75; 0.51-1.08). Analysis adjusted for aspirin use and traditional **cardiovascular risk** factors had no significant effect on these findings. CONCLUSION: In a large prospective cohort, carriage of the T allele for the C148T mutation in the beta-fibrinogen promoter gene was not associated with an increased subsequent **risk** of **cardiovascular** events.

L2 ANSWER 58 OF 80 MEDLINE on STN
Full Text
AN 2001555309 MEDLINE
DN PubMed ID: 11602206
TI Variations of **cardiovascular** disease associated genes exhibit

sex-dependent influence on human longevity.
AU Tan Q; Yashin A I; Bladbjerg E M; de Maat M P; Andersen-Ranberg K; Jeune B; Christensen K; Vaupel J W
CS Max-Planck Institute for Demographic Research, Rostock, Germany.
SO Experimental gerontology, (2001 Aug) Vol. 36, No. 8, pp. 1303-15. Journal code: 0047061. ISSN: 0531-5565.
CY England: United Kingdom
DT (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 17 Oct 2001
Last Updated on STN: 22 Jan 2002
Entered Medline: 7 Dec 2001
AB This article investigates the relationship between the polymorphic variations in genes associated with **cardiovascular** disease and longevity in the Danish population. A new procedure that combines both demographic and the individual genetic information in determining the **relative risks** of the observed genetic variations is applied. The sex-dependent influences can be found by introducing sex-specific population survival and incorporating the **risk** of gene-sex interaction. Three genetic polymorphisms, angiotensinogen M/T235, blood coagulation factor VII (FVII) R/Q353 and FVII-323ins10, manifest significant influences on survival in males, with reduced hazards of death for carriers of the angiotensinogen M235 allele, the F VII Q353 allele, and the FVII-323P10 allele. The results show that some of these **genotypes** associated with lower **risk** of **CVD** could also reduce the carrier's death rate and contribute to longevity. However, the presence of sex-dependent effects and the fact that major **CVD**-associated genes failed to impose detrimental influence on longevity lead us to concur that the aging process is highly complicated.

L2 ANSWER 59 OF 80 MEDLINE on STN
Full Text
AN 2001535461 MEDLINE
DN PubMed ID: 11583310
TI **Risk** of pregnancy-related venous thrombosis in carriers of severe inherited thrombophilia.
AU Martinelli I; Legnani C; Bucciarelli P; Grandone E; De Stefano V; Mannucci P M
CS Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, IRCCS Maggiore Hospital, University of Milan, Italy.. martin@polic.cilea.it
SO Thrombosis and haemostasis, (2001 Sep) Vol. 86, No. 3, pp. 800-3. Journal code: 7608063. ISSN: 0340-6245.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE) (MULTICENTER STUDY) (CLINICAL TRIAL)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 4 Oct 2001
Last Updated on STN: 9 Apr 2002
Entered Medline: 8 Apr 2002
AB Homozygous carriers of factor V Leiden have an approximately 80-fold increased **risk** of venous thrombosis. Also double heterozygous carriers of both the factor V Leiden and the prothrombin gene mutations are at high thrombotic **risk**. The magnitude of the **risk** of venous thrombosis in pregnant women with the two severe thrombophilic conditions has not been estimated so far. We performed a multicenter retrospective family study in women with homozygous factor V Leiden, double heterozygous factor V Leiden and the prothrombin gene mutation, and women with normal coagulation. Only relatives of index patients with thrombosis formed the study cohort. Fifteen homozygous and 39 double heterozygous women were compared to 182 women with normal coagulation. Venous thrombosis occurred in 3 of 19, 2 of 50 and 1 of 221 pregnancies, respectively. One thrombotic episode occurred in the third trimester, the remaining 5 in the postpartum. The prevalence of venous thrombosis was 15.8% (95% CI 3.4-39.6) for homozygotes. 4.0% (95% CI 0.5-13.7) for double heterozygotes and 0.5% for women with normal coagulation. The **relative risk** of pregnancy-related venous thrombosis was 41.3 (95% CI 4.1-419.7) for

homozygous and 9.2 (95% CI 0.8-103.2) for double heterozygous carriers. In conclusion, homozygous carriers of factor V Leiden and, to a lesser extent, double heterozygous carriers of factor V Leiden and of the prothrombin mutation have an increased **risk** of venous thrombosis during pregnancy, particularly high during the postpartum period. On the basis of these findings we recommend that these women receive anticoagulant prophylaxis at least in the postpartum, that should perhaps be extended to the whole pregnancy in homozygous carriers.

L2 ANSWER 60 OF 80 MEDLINE on STN
Full Text
AN 2001435118 MEDLINE
DN PubMed ID: 11303694
TI Methylenetetrahydrofolate reductase gene polymorphism and **risk** of premature myocardial infarction.
AU Gulec S; Aras O; Akar E; Tutar E; Omurlu K; Avci F; Dincer I; Akar N; Oral D
CS Medical School of Ankara University, Turkey.
SO Clinical cardiology, (2001 Apr) Vol. 24, No. 4, pp. 281-4.
Journal code: 7903272. ISSN: 0160-9289.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200108
ED Entered STN: 6 Aug 2001
Last Updated on STN: 6 Aug 2001
Entered Medline: 2 Aug 2001
AB BACKGROUND: Elevated plasma homocysteine level is an independent **risk** factor for **cardiovascular** disease. A common mutation (nucleotid 677C-T) in the gene coding for methylenetetrahydrofolate reductase (MTHFR) has been reported to reduce the enzymatic activity of MTHFR and is associated with elevated plasma levels of homocysteine, especially in subjects with low folate intake. HYPOTHESIS: Methylenetetrahydrofolate reductase T/T **genotype** may be a **risk** factor for premature MI in Turkish population who are known to have low folate levels. METHODS: The study group was comprised of 96 men (aged <45 years) with premature myocardial infarction (MI) and 100 age- and gender-matched controls who had no history or clinical evidence of coronary artery disease (CAD) and/or MI. DNA was extracted from peripheral blood and **genotypes** were determined by polymerase chain reaction, restriction mapping with HinfI, and gel electrophoresis. Conventional **risk** factors for CAD were prospectively documented. RESULTS: Allele and **genotype** frequencies among cases and control subjects were compatible with Hardy-Weinberg equilibrium. The frequencies of T/T, C/T, and C/C **genotypes** among patients with MI and control subjects were 15.6, 40.6, and 43.8%, and 5, 35, and 60%, respectively. Multivariate analyses identified smoking, MTHFR C/T polymorphism, diabetes mellitus, family history of CAD, and hypertension as the independent predictors of premature MI. Defining patients with non-T/T **genotype** (C/C and C/T combined) as reference, the **relative risk** of MI for subjects with T/T **genotype** was 5.94 (95% confidence interval: 1.96-18.02, p = 0.0016). CONCLUSIONS: Our findings suggest that C677T transition in the MTHFR gene may be a **risk** factor for premature MI in Turkish men.

L2 ANSWER 61 OF 80 MEDLINE on STN
Full Text
AN 2001196287 MEDLINE
DN PubMed ID: 11246885
TI A polymorphism in the gene for IGF-I: functional properties and **risk** for type 2 diabetes and myocardial infarction.
AU Vaessen N; Heutink P; Janssen J A; Witteman J C; Testers L; Hofman A; Lamberts S W; Oostra B A; Pols H A; van Duijn C M
CS Department of Epidemiology and Biostatistics, the Center for Biomedical Genetics, Rotterdam, The Netherlands.
SO Diabetes, (2001 Mar) Vol. 50, No. 3, pp. 637-42.
Journal code: 0372763. ISSN: 0012-1797.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals

EM 200104
ED Entered STN: 10 Apr 2001
Last Updated on STN: 10 Apr 2001
Entered Medline: 5 Apr 2001
AB Evidence is accumulating that low levels of IGF-I play a role in the pathogenesis of type 2 diabetes and **cardiovascular** diseases. We examined the role of a genetic polymorphism in the promoter region of the IGF-I gene in relation to circulating IGF-I levels and growth measured as body height, and we studied the relationship of this polymorphism with type 2 diabetes and myocardial infarction. The relation between the IGF-I polymorphism and body height was assessed in a population-based sample of 900 subjects from the Rotterdam Study. Within each **genotype** stratum, 50 subjects were randomly selected for a study of the relation of this polymorphism with serum IGF-I levels. To assess the **risk** for type 2 diabetes, we studied 220 patients and 596 normoglycemic control subjects. For myocardial infarction, 477 patients with evidence of myocardial infarction on electrocardiogram and 808 control subjects were studied. A 192-bp allele was present in 88% of the population, suggesting that this is the wild-type allele from which all other alleles originated. Body height was, on average, 2.7 cm lower (95% CI for difference -4.6 to -0.8 cm, P = 0.004), and serum IGF-I concentrations were 18% lower (95% CI for difference -6.0 to -1.3 mmol/l, P = 0.003) in subjects who did not carry the 192-bp allele. In noncarriers of the 192-bp allele, an increased **relative risk** for type 2 diabetes (1.7 [95% CI 1.1-2.7]) and for myocardial infarction (1.7 [95% CI 1.1-2.5]) was found. In patients with type 2 diabetes, the **relative risk** for myocardial infarction in subjects without the 192-bp allele was 3.4 (95% CI 1.1-11.3). Our study suggests that a genetically determined exposure to relatively low IGF-I levels is associated with an increased **risk** for type 2 diabetes and myocardial infarction.

L2 ANSWER 62 OF 80 MEDLINE on STN
Full Text
AN 2001047748 MEDLINE
DN PubMed ID: 10998471
TI The paraoxonase Leu-Met54 and Gln-Arg191 gene polymorphisms are not associated with the **risk** of coronary heart disease.
AU Gardemann A; Philipp M; Hess K; Katz N; Tillmanns H; Haberbosch W
CS Institut fur Klinische Chemie und Pathobiochemie, Klinikum der Justus-Liebig-Universitat Giessen, Gaffky-Strasse 11, 35392, Giessen, Germany.
SO Atherosclerosis, (2000 Oct) Vol. 152, No. 2, pp. 421-31.
Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200012
ED Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 7 Dec 2000
AB BACKGROUND: Evidence has been presented that gene polymorphisms (PON54 L/M, PON191 Q/R) of paraoxonase are **risk** factors of coronary heart disease. RESULTS: We determined both PON **genotypes** in 535 male individuals who were free of vascular disease and in 2249 male subjects who underwent coronary angiography, and analysed the relation of both gene variations to CAD and MI. Both gene polymorphisms were in linkage disequilibrium (P<0.0001). Coronary artery disease: the PON54 gene polymorphism was not associated with an increased **risk** of CAD. In the total sample and also in younger subjects, an association of the PON191 gene variation with the **risk** of CAD was not detected when the control group of individuals without coronary heart disease was compared with patients with at least one diseased vessel (verified by coronary angiography). In individuals younger than 62 years, a moderate increase in the **relative risk** of CAD associated with the PON191 R allele (1.45 (1. 08-1.95); P=0.015) were found, when subjects without vessel disease (verified by coronary angiography) were compared with CAD patients. Myocardial infarction: an association of the PON54 gene variation with MI was not detected when the control group of individuals without coronary heart disease were compared with patients with at least one MI. A marginal increase in the **risk** of MI associated with the PON54 LL **genotype** (OR 1.27 (1.05-1.51); P=0.011) were detected when patients

without MI but with coronary angiography were compared with MI positive patients. Subgroup analyses of low- and high-**risk** populations did not reveal any association of both PON gene polymorphisms with CAD or MI. CONCLUSION: The present findings do not strengthen the hypothesis that the paraoxonase gene polymorphisms are independently associated with coronary heart disease indicating that these gene variations are of little usefulness as genetic markers of **cardiovascular** disease.

L2 ANSWER 63 OF 80 MEDLINE on STN
Full Text
AN 2000403091 MEDLINE
DN PubMed ID: 10837089
TI Analysis of CYP21 coding polymorphisms in three ethnic populations: further evidence of nonamplifying CYP21 alleles among whites.
AU Ozturk I C; Wei W L; Palaniappan L; Rubenfire M; Killeen A A
CS Department of Pathology, University of Michigan Medical School, Ann Arbor, MI 48109, USA.
SO Molecular diagnosis : a journal devoted to the understanding of human disease through the clinical application of molecular biology, (2000 Mar) Vol. 5, No. 1, pp. 47-52.
Journal code: 9614965. ISSN: 1084-8592.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 1 Sep 2000
Last Updated on STN: 1 Sep 2000
Entered Medline: 21 Aug 2000
AB BACKGROUND: Adrenal steroid 21-hydroxylase is essential for the synthesis of both mineralocorticoids and glucocorticoids. The gene for this enzyme, CYP21, contains several frequent coding polymorphisms. Because of its essential function in steroid synthesis, polymorphisms in this enzyme might influence a variety of disease processes. However, before disease-association studies are performed, it is important to understand the frequency of these polymorphisms among normal individuals. METHODS: Using polymerase chain reaction (PCR) with restriction enzyme digestion or size length polymorphism analysis, we measured the frequencies of the +Leu(10), Arg102Lys, and Ser268Thr polymorphisms in CYP21 in healthy whites, blacks, and Indian Americans. The subjects were all young female college students participating in a study of **relative risks** for **cardiovascular** disease in these populations. RESULTS: The frequency of each polymorphism among whites, blacks, and Indian Americans were as follows: +Leu(10), 0.55, 0.96, 0.75; Arg102, 0.63, 0.97, 0.82; and Ser268, 0.92, 0.68, 0.79, respectively. With the exception of the frequencies of the Ser268Thr polymorphism among blacks and Indian Americans, there were significantly different frequencies of each polymorphism among all groups ($P<.05$). Among whites, the distribution of **genotypes** for the +Leu(10) and Arg102Lys polymorphisms deviated significantly from expected Hardy-Weinberg values because of an excess of homozygotes. CONCLUSIONS: Among the ethnic groups, there are statistically significant differences in the frequencies of these common coding polymorphisms in CYP21 that need to be considered in disease-association studies. Deviation from Hardy-Weinberg distributions might be explained by allelic dropout during PCR, a phenomenon previously reported at this locus.

L2 ANSWER 64 OF 80 MEDLINE on STN
Full Text
AN 2000086782 MEDLINE
DN PubMed ID: 10618306
TI Plasminogen activator inhibitor 4G polymorphism is associated with decreased **risk** of cerebrovascular mortality in older women.
AU Roest M; van der Schouw Y T; Banga J D; Tempelman M J; de Groot P G; Sixma J J; Grobbee D E
CS Julius Center for Patient Oriented Research, Department of Hematology, Graduate School of Biomembranes, Utrecht University Medical School, Netherlands.. M.Roest@jc.azu.nl
SO Circulation, (Jan 4-11 2000) Vol. 101, No. 1, pp. 67-70.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Abridged Index Medicus Journals; Priority Journals
EM 200002
ED Entered STN: 9 Mar 2000
Last Updated on STN: 9 Mar 2000
Entered Medline: 24 Feb 2000
AB BACKGROUND: A common 4G allele of a 4G/5G polymorphism in the promoter region of the plasminogen activator inhibitor-1 (PAI-1) gene is associated with increased transcription of the PAI-1 protein, which may lead to decreased fibrinolysis. It has therefore been proposed as a candidate **risk** factor for myocardial infarction or stroke. METHODS AND RESULTS: We studied the relationship between PAI-1 4G/5G **genotype** and the **risk** of **cardiovascular** mortality in a prospective cohort study among 12 239 women initially aged between 52 and 67 years, with a maximum follow-up time of 18 years (153 732 follow-up years). PAI-1 4G/5G **genotype** was measured in DNA obtained from urine samples, which were collected at baseline, of 498 women who died of a **cardiovascular** disease and a random sample of 512 women from the same cohort who did not die of **cardiovascular** disease. The PAI-1 4G/5G **genotype** was not associated with **risk** of myocardial infarction or other **cardiovascular** mortality. However, PAI-1 4G4G homozygotes had a markedly reduced **risk** of cerebrovascular mortality compared with PAI-1 5G5G homozygotes: the **relative risk** was 0.4, with a 95% CI of 0.2 to 0.7, whereas the **relative risk** of cerebrovascular mortality in PAI-1 4G5G heterozygotes compared with PAI-1 5G5G homozygotes was 0.7, with a 95% CI of 0.4 to 1.1. CONCLUSIONS: These findings are suggestive of an important contribution of PAI-1 in cerebrovascular pathology, probably via pathways other than fibrinolysis. PAI-1 may protect against destabilization of the atherosclerotic plaque, or it may inhibit neurotoxicity of tissue plasminogen activator in the brain.

L2 ANSWER 65 OF 80 MEDLINE on STN
Full Text
AN 2000051392 MEDLINE
DN PubMed ID: 10582985
TI Association of the platelet glycoprotein IIb HPA-3 polymorphism with survival after acute ischemic stroke.
AU Carter A M; Catto A J; Bamford J M; Grant P J
CS Unit of Molecular Vascular Medicine, Research School of Medicine, University of Leeds, Leeds General Infirmary, and Department of Neurology, St. James' University Hospital, Leeds, UK.
SO Stroke; a journal of cerebral circulation, (1999 Dec) Vol. 30, No. 12, pp. 2606-11.
Journal code: 0235266. ISSN: 0039-2499.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 13 Jan 2000
Last Updated on STN: 13 Jan 2000
Entered Medline: 10 Dec 1999
AB BACKGROUND AND PURPOSE: The role of polymorphisms of the platelet glycoprotein (GP) IIb/IIIa receptor in the development of **cardiovascular** disease has been the subject of intensive research. The aim of this study was to determine the association of the HPA-3 polymorphism of platelet GPIIb with ischemic stroke and subsequent survival and to identify possible interactions of HPA-3 with classic **risk** factors. METHODS: HPA-3 **genotype** was determined by restriction fragment length polymorphism in 515 patients with ischemic stroke and 423 healthy, age-matched control subjects. RESULTS: There was no significant difference in the **genotype** distribution of patients and controls, nor was there any difference when patients were subclassified into small- and large-vessel disease. The **genotype** distribution of the 231 patients subsequently dying during 2.8 years of follow-up (aa=45.0%, ab=46.8%, bb=8.2%) was significantly different from that of those still alive (aa=37.0%, ab=48.2%, bb=14. 8%) (P=0.03). In a Cox regression model, the **relative risks** for poststroke mortality in patients of aa and ab **genotype** compared with those of bb **genotype** were 2.42 (95% CI, 1.24 to 4.71) and 2.13 (95% CI, 1.09 to 4.17), respectively, after we accounted for confounding factors. In addition, significant interactions of HPA-3 with the Pl(A) polymorphism of GPIIIa (P=0.002) and with fibrinogen

(P=0.01) were identified in relation to mortality. CONCLUSIONS: HPA-3 is related to poststroke mortality, and the significant interaction of HPA-3 with Pl(A) and fibrinogen suggests that it may in some way influence the interaction of GPIIb/IIIa with fibrinogen, particularly in the presence of high fibrinogen.

L2 ANSWER 66 OF 80 MEDLINE on STN
Full Text
AN 1999449119 MEDLINE
DN PubMed ID: 10520809
TI Angiotensin I-converting enzyme and plasminogen activator inhibitor-1 gene variants: **risk** of mortality and fatal **cardiovascular** disease in an elderly population-based cohort.
AU Heijmans B T; Westendorp R G; Knook D L; Kluft C; Slagboom P E
CS Gaubius Laboratory, TNO Prevention and Health, Leiden, The Netherlands.
NC AG06354 (United States NIA)
SO Journal of the American College of Cardiology, (1999 Oct) Vol. 34, No. 4, pp. 1176-83.
Journal code: 8301365. ISSN: 0735-1097.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199910
ED Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 27 Oct 1999
AB OBJECTIVES: We studied the contribution of putative **risk genotypes** at the angiotensin I-converting enzyme inhibitor (ACE D/D) and plasminogen activator inhibitor-1 (PAI-1 4G/4G) loci to all-cause and **cardiovascular** mortality in a population-based cohort. BACKGROUND: The ACE D/D and PAI-1 4G/4G **genotypes** have been consistently associated with elevated plasma activities of the gene products. Their role in **cardiovascular** disease, although explored intensively, is still equivocal. METHODS: The ACE and PAI-1 **genotypes** were determined in 648 subjects > or =85 years old. In a cross-sectional analysis, the **genotype** distributions in a subset of 356 elderly subjects who were born in Leiden, The Netherlands, were compared with those in 250 young subjects whose families originated from the same geographic region. In addition, the complete cohort of elderly subjects was followed over 10 years for all-cause and **cardiovascular** mortality and was stratified according to **genotype**. RESULTS: In the cross-sectional analysis, the ACE and PAI-1 **genotype** distributions were similar in elderly and young subjects. In the prospective follow-up study, however, the age-adjusted **risk** of fatal ischemic heart disease was increased threefold (95% confidence interval [CI] 1.2 to 7.6) in elderly men carrying the PAI-1 4G/4G **genotype**. The **risk** of all-cause mortality was not increased among elderly subjects carrying the PAI-1 4G/4G (**relative risk** [RR] 0.9, 95% CI 0.7 to 1.1) or the ACE D/D **genotype** (RR 0.9, 95% CI 0.7 to 1.1), nor did we observe elevated **risks** of death from all **cardiovascular** diseases combined. There was no interaction between the **genotypes**. CONCLUSIONS: The PAI 4G/4G **genotype** may be a **risk** factor for fatal ischemic heart disease in elderly men. The impact of moderately increased ACE and PAI-1 activities associated with the ACE D/D and PAI-1 4G/4G **genotypes** is too small to affect mortality in the general population.

L2 ANSWER 67 OF 80 MEDLINE on STN
Full Text
AN 1999438104 MEDLINE
DN PubMed ID: 10506586
TI **Genotyping** and functional analysis of a polymorphic (CCTTT)(n) repeat of NOS2A in diabetic retinopathy.
AU Warpeha K M; Xu W; Liu L; Charles I G; Patterson C C; Ah-Fat F; Harding S; Hart P M; Chakravarthy U; Hughes A E
CS Department of Medical Genetics, Ophthalmology and Vision Sciences, Queen's University, Belfast, UK.
SO The FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (1999 Oct) Vol. 13, No. 13, pp. 1825-32.
Journal code: 8804484. ISSN: 0892-6638.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199911
ED Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 2 Nov 1999
AB Accumulating evidence shows that the severity and rapidity of onset of diabetic retinopathy are influenced by genetic factors. Expression of the nitric oxide synthases is altered in the retinal vasculature in the early stages of diabetic retinopathy. We analyzed the allele distribution of a polymorphic pentanucleotide repeat within the 5' upstream promoter region of the NOS2A gene in samples of diabetic patients. In diabetic patients from Northern Ireland, the 14-repeat allele of the NOS2A marker was significantly associated with the absence of diabetic retinopathy. Carriers of this repeat had 0.21-fold the **relative risk** of developing diabetic retinopathy than noncarriers of this allele. They also had significantly fewer renal and **cardiovascular** complications. The ability of differing numbers of (CCTTT)(n) pentanucleotide repeats to induce transcription of the NOS2A gene was analyzed using a luciferase reporter gene assay in transfected colonic carcinoma cells. Interleukin 1beta (IL-1beta) induction was most effective in constructs carrying the 14-repeat allele. When cells were incubated in 25 mM glucose to mimic the diabetic state, IL-1beta induction was inhibited in all cases, but to a significantly lesser extent with the 14-repeat allele. These unique properties of the 14-repeat allele may confer selective advantages in diabetic individuals, which may delay or prevent microvascular complications of diabetes.

L2 ANSWER 68 OF 80 MEDLINE on STN
Full Text
AN 1999327036 MEDLINE
DN PubMed ID: 10398289
TI A frailty approach for modelling diseases with variable age of onset in families: the NHLBI Family Heart Study.
AU Siegmund K D; Todorov A A; Province M A
CS Department of Preventive Medicine, University of Southern California, Los Angeles 90033, USA.. kims@rcf.usc.edu
NC CA-52862 (United States NCI)
GM-28719 (United States NIGMS)
HL-56567 (United States NHLBI)
+
SO Statistics in medicine, (1999 Jun 30) Vol. 18, No. 12, pp. 1517-28.
Journal code: 8215016. ISSN: 0277-6715.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 25 Sep 1999
Last Updated on STN: 25 Sep 1999
Entered Medline: 9 Sep 1999
AB We use frailty models to analyse the effect of latent genetic and environmental **risk** factors on hazard functions in nuclear families. The approach expresses latent **risk** factors (frailties) as functions of the effects of a single major gene and shared familial **risk**. The latter may result from shared polygenes and/or a common environment. Genetic frailties are modelled using a two-point distribution, and residual frailties (shared environment, polygenes) using a gamma distribution. The two-point distribution follows the laws of Mendelian transmission, under either dominant or recessive gene action. We describe a robust EM approach for the joint estimation of the magnitude of genetic, covariate, gene by covariate interaction effects while allowing residual familial correlation. We illustrate the method on coronary heart disease data from the National Heart, Lung, and Blood Institute Family Heart Study. In addition, a simulation study shows that ignoring possible residual correlation in disease status due to a shared familial environment leads to an overestimate of the **relative risk** associated with a latent **genotype**.

L2 ANSWER 69 OF 80 MEDLINE on STN
Full Text
AN 1999117312 MEDLINE
DN PubMed ID: 9918518
TI Prospective evaluation of the angiotensin-converting enzyme insertion/deletion polymorphism and the **risk** of stroke.
AU Zee R Y; Ridker P M; Stampfer M J; Hennekens C H; Lindpaintner K
CS Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Boston, Mass 02115, USA.. rylz@calvin.bwh.harvard.edu
NC CA-40360 (United States NCI)
K04-HL-03138-01 (United States NHLBI)
R01-HL-56411-01 (United States NHLBI)
+
SO Circulation, (1999 Jan 26) Vol. 99, No. 3, pp. 340-3.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199902
ED Entered STN: 23 Feb 1999
Last Updated on STN: 23 Feb 1999
Entered Medline: 11 Feb 1999
AB BACKGROUND: The D/I polymorphism of the ACE gene has been studied in relation to a variety of **cardiovascular** disorders, including stroke. A number of small studies have been conducted, with inconsistent results. We investigated the association between ACE **genotype** and the incidence of stroke in a large, prospective, matched case-control sample from the Physicians' Health Study. METHODS AND RESULTS: In the Physicians' Health Study, 348 subjects who had been apparently healthy at enrollment suffered a stroke during 12 years of follow-up, as determined from medical records and autopsy. A total of 348 cases were matched by age, time of randomization, and smoking habit to an equal number of controls (who had remained free of stroke). The D/I polymorphism was determined by polymerase chain reaction. Data were analyzed for the entire nested case-control sample, and also among a subgroup without a history of hypertension or diabetes mellitus, considered to be at low conventional **risk** (207 cases and 280 controls). All observed **genotype** frequencies were in Hardy-Weinberg equilibrium. The **relative risk** associated with the D allele was 1.11 (95% CI, 0.90 to 1.37; P=0.35), assuming an additive model in the matched analysis. Additional analyses assuming dominant or recessive effects of the D allele, as well as the analysis after stratification for low-**risk** status, showed no material as a statistically significant association. CONCLUSIONS: The results of this large, prospective study indicate that the ACE D/I gene polymorphism is not associated with subsequent **risk** of stroke.

L2 ANSWER 70 OF 80 MEDLINE on STN
Full Text
AN 1999060160 MEDLINE
DN PubMed ID: 9843457
TI Common methylenetetrahydrofolate reductase gene mutation leads to hyperhomocysteinemia but not to vascular disease: the result of a meta-analysis.
AU Brattstrom L; Wilcken D E; Ohrvik J; Brudin L
CS Department of Medicine, County Hospital, Kalmar, Sweden.. lars.brattstrom@alinks.se
SO Circulation, (1998 Dec 8) Vol. 98, No. 23, pp. 2520-6.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(META-ANALYSIS)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199901
ED Entered STN: 15 Jan 1999
Last Updated on STN: 28 Jul 2000
Entered Medline: 4 Jan 1999

AB BACKGROUND: The results of retrospective and prospective case-control studies have clearly established that mild elevations of the plasma homocysteine level are associated with increased **risk** of coronary, cerebral, and peripheral vascular disease. Recently, a mutation (677C-->T) was identified in the methylenetetrahydrofolate reductase (MTHFR) gene that results in reduced folate-dependent enzyme activity and reduced remethylation of homocysteine to methionine. Mutant homozygotes (TT **genotype**) constitute approximately 12% of the white population and frequently have mildly elevated circulating homocysteine. Therefore, it seems likely that they would also be at increased **risk** of vascular disease. A number of studies have investigated this during the past 3 years, and the present article evaluates the results in a meta-analysis. METHODS AND RESULTS: We identified 13 studies in which there were measurements of plasma homocysteine in relation to the 3 **genotypes** (TT, CT, and CC) and 23 case-control studies comprising 5869 **genotyped** **cardiovascular** disease patients (mostly coronary artery disease) and 6644 **genotyped** control subjects. Those bearing the TT **genotype** had plasma homocysteine concentrations 2.6 micromol/L (25%) higher than those with the CC **genotype**. However, there was no difference between patients and control subjects either in the frequency of mutant alleles (T) (34.3% versus 33.8%) or the TT **genotype** (11.9% versus 11.7%). In the analysis of the 23 studies, the **relative risk** (OR) of vascular disease associated with the TT **genotype** was 1.12 (95% CI, 0.92 to 1.37). CONCLUSIONS: We conclude that although the C677T/MTHFR mutation is a major cause of mild hyperhomocysteinemia, the mutation does not increase **cardiovascular risk**. Our findings suggest that the mild hyperhomocysteinemia found frequently in vascular disease patients is not causally related to the pathogenesis of the vascular disease.

L2 ANSWER 71 OF 80 MEDLINE on STN
Full Text
AN 1998370380 MEDLINE
DN PubMed ID: 9706883
TI **Risk** of left ventricular dysfunction in patients with probable Alzheimer's disease with APOE*4 allele.
AU van der Cammen T J; Verschoor C J; van Loon C P; van Harskamp F; de Koning I; Schudel W J; Slooter A J; Van Broeckhoven C; van Duijn C M
CS Department of Internal Medicine I and Geriatric Medicine, Erasmus University Medical School, Rotterdam, The Netherlands.
SO Journal of the American Geriatrics Society, (1998 Aug) Vol. 46, No. 8, pp. 962-7.
Journal code: 7503062. ISSN: 0002-8614.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 3 Sep 1998
Last Updated on STN: 3 Sep 1998
Entered Medline: 26 Aug 1998
AB OBJECTIVE: To examine the association between the APOE **genotype** and **cardiovascular** disease in Alzheimer's disease (AD) patients. DESIGN: Case register study of 100 consecutive referrals to a Memory Clinic where type of dementia and **cardiovascular** comorbidity were diagnosed and APOE **genotype** was determined. SETTING: The Memory Clinic, University Hospital Rotterdam Dijkzigt. PARTICIPANTS: One hundred Memory Clinic patients, 59 to 91 years of age, who attended the Memory Clinic in the period between January 1994 and March 1996. MEASUREMENTS: **Relative** **risk** of **cardiovascular** morbidity in probable AD, based on clinical and ECG findings. RESULTS: The diagnosis of probable AD was more frequent in APOE*4 allele-carrying AD patients. When comparing homozygotes for APOE*4 with homozygotes for APOE*3, a nine-fold increase in prevalence of cardiac ischemia on ECG was found in the former. When grouping parameters of left ventricular dysfunction, the prevalence was 7.2 (95% confidence interval 1.2-42.6) times greater in probable Alzheimer patients with APOE4/4. CONCLUSIONS: In patients with probable AD, APOE*4 is associated with cardiac disease indicative of left ventricular dysfunction.

L2 ANSWER 72 OF 80 MEDLINE on STN
Full Text
AN 1998147550 MEDLINE
DN PubMed ID: 9488226

TI Alpha-adducin gene polymorphism and **cardiovascular** phenotypes in a general population.
AU Castellano M; Barlassina C; Muiesan M L; Beschi M; Cinelli A; Rossi F; Rizzoni D; Cusi D; Agabiti-Rosei E
CS Department of Medical Sciences, University of Brescia, Italy.
SO Journal of hypertension, (1997 Dec) Vol. 15, No. 12 Pt 2, pp. 1707-10. Journal code: 8306882. ISSN: 0263-6352.
CY ENGLAND: United Kingdom
DT (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 10 Apr 1998
Last Updated on STN: 10 Apr 1998
Entered Medline: 2 Apr 1998
AB BACKGROUND: Previous studies have shown that molecular variants of the cytoskeletal protein adducin may be involved in regulation of blood pressure both in genetic rat hypertension and in human essential hypertension. OBJECTIVE: To investigate the relationship of genetic polymorphism of alpha-adducin with blood pressure, **cardiovascular** structure, and some biochemical indexes of **cardiovascular risk** in a sample of general population. DESIGN AND METHODS: A sample of 246 subjects (124 men and 122 women, aged 57.7+/-3.7 years) was randomly chosen from a middle-aged population. Twenty-four-hour ambulatory blood pressure, as well as left ventricular mass (by echocardiographic methods) and carotid wall thickness (by B-mode ultrasound methods) were measured. DNA was extracted from peripheral blood samples; the Gly460Trp diallelic variant of human alpha-adducin was **genotyped** by polymerase chain reaction amplification and then allele-specific oligo hybridization. RESULTS: A trend toward higher 24 h ambulatory blood pressure values in subjects not treated with antihypertensive drugs was observed among carriers of Trp460 allele, although the differences did not attain statistical significance (at closest, P = 0.066 for a dominant effect of Trp460 on systolic blood pressure). When blood pressure was considered a dichotomous variable, allowing the inclusion of treated hypertensives), a higher prevalence of Trp460 allele among hypertensives was observed (0.188 versus 0.106 among normotensives, P= 0.02). There was no evidence of association either of left ventricular mass or of common carotid wall thickness with Gly460Trp polymorphism. CONCLUSIONS: In this sample of a general population, the relationship of a genetic polymorphism of alpha-adducin with blood pressure values was rather weak. However, a population-based case-control analysis indicated that there was an association between Trp460 allele and hypertension, with a **relative risk** for subjects carrying at least one Trp460 allele of approximately 1.6. Further investigation of larger and different population samples in order to assess the role of adducin gene polymorphism as a marker of genetic predisposition to the development of hypertension is warranted.

L2 ANSWER 73 OF 80 MEDLINE on STN
Full Text
AN 1998104012 MEDLINE
DN PubMed ID: 9443775
TI Polymorphism of angiotensin converting enzyme, angiotensinogen, and apolipoprotein E genes in a Japanese population with cerebrovascular disease.
AU Nakata Y; Katsuya T; Rakugi H; Takami S; Sato N; Kamide K; Ohishi M; Miki T; Higaki J; Ogihara T
CS Department of Geriatric Medicine, Osaka University Medical School, Suita, Japan.
SO American journal of hypertension : journal of the American Society of Hypertension, (1997 Dec) Vol. 10, No. 12 Pt 1, pp. 1391-5. Journal code: 8803676. ISSN: 0895-7061.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
ED Entered STN: 26 Feb 1998
Last Updated on STN: 26 Feb 1998
Entered Medline: 19 Feb 1998
AB The homozygous deletion allele of the angiotensin converting enzyme gene

(ACE/DD), homozygous threonine allele of the angiotensinogen gene (AGN/TT), and the epsilon4 allele of the apolipoprotein E gene (apoE/epsilon4) are reported to be associated with ischemic heart disease. Cerebrovascular disease (**CVD**) is another atherosclerotic disease; and the effects of these polymorphisms on **CVD** have been confusing. In this study, we investigated whether ACE/DD, AGN/TT, and apoE/epsilon4 **genotypes** are associated with **CVD** and whether genetic **risk** is enhanced by the effect of one upon another. We ascertained these **genotypes** in patients with cerebral infarction (n = 55) and cerebral hemorrhage (n = 38), diagnosed by brain computed tomography. Control subjects for the infarction group and the hemorrhage group were randomly selected from 583 subjects matched for age, gender, and history of hypertension with patients. Frequency of ACE/DD **genotype** was higher in the patients with infarction than in the controls (chi2 = 6.1, P < .05). The AGN/TT **genotype** was not associated with either infarction or hemorrhage, but it increased the **relative risk** for cerebral infarction in the subjects with ACE/DD **genotype** (chi2 = 8.0, P < .01, odds ratio; 11.7, 95% confidence intervals: 1.4 to 96.0). There was no significant association between apoE/epsilon4 and **CVD**. These results suggest that ACE/DD predicts cerebral infarction, but not cerebral hemorrhage, and that AGN/TT enhances the **risk** for cerebral infarction associated with ACE/DD.

L2 ANSWER 74 OF 80 MEDLINE on STN
Full Text
AN 1997468699 MEDLINE
DN PubMed ID: 9327764
TI Alu-repeat polymorphism in the gene coding for tissue-type plasminogen activator (t-PA) and **risks** of myocardial infarction among middle-aged men.
AU Ridker P M; Baker M T; Hennekens C H; Stampfer M J; Vaughan D E
CS Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA.. pmridker@bics.bwh.harvard.edu
SO Arteriosclerosis, thrombosis, and vascular biology, (1997 Sep) Vol. 17, No. 9, pp. 1687-90.
Journal code: 9505803. ISSN: 1079-5642.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
ED Entered STN: 24 Dec 1997
Last Updated on STN: 29 Jan 1999
Entered Medline: 13 Nov 1997
AB An Alu-repeat polymorphism in the gene coding for tissue-type plasminogen activator has been described recently, and it has been hypothesized that this polymorphism may predict **risk** of coronary thrombosis. In a prospective cohort of nearly 15,000 apparently healthy men, presence of an Alu-repeat insertion/deletion (I/D) polymorphism in the gene coding for tissue-type plasminogen activator was determined among 369 study participants who subsequently suffered a first myocardial infarction (cases) and among a group of 369 age- and smoking-matched study participants who remained free of reported **cardiovascular** disease during follow-up (controls). The distributions of the II, DI, and DD **genotypes** of the tissue-type plasminogen activator polymorphism among men who subsequently suffered myocardial infarction (0.30, 0.50, 0.21) were virtually identical to those who remained free of disease (0.29, 0.50, 0.21; P = .9). There was no evidence of association between the Alu insertion polymorphism and **risks** of future myocardial infarction in models assuming either allelic recessive (**relative risk**, 1.05; 95% confidence interval, 0.8 to 1.4, P = .8) or allelic dominant (**relative risk**, 1.04; 95% confidence interval, 0.7 to 1.5, P = .8) modes of inheritance, nor were associations found in analyses stratified by age, family history, hypercholesterolemia, or the presence of other **risk** factors for premature coronary disease. Multivariate analysis had no important effects on these relationships. In this cohort of middle-aged US men, the presence of the insertion allele of the Alu-repeat polymorphism of the tissue-type plasminogen activator gene is not associated with future **risks** of myocardial infarction.

L2 ANSWER 75 OF 80 MEDLINE on STN
Full Text
AN 1997436534 MEDLINE

DN PubMed ID: 9292507
TI A common prothrombin variant (20210 G to A) increases the **risk** of myocardial infarction in young women.
AU Rosendaal F R; Siscovick D S; Schwartz S M; Psaty B M; Raghunathan T E; Vos H L
CS Department of Clinical Epidemiology, University Hospital Leiden, The Netherlands.
NC N01-HD-1-3107 (United States NICHD)
SO Blood, (1997 Sep 1) Vol. 90, No. 5, pp. 1747-50.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199709
ED Entered STN: 13 Oct 1997
Last Updated on STN: 13 Oct 1997
Entered Medline: 30 Sep 1997
AB Using specimens from a population-based case control study among women ages 18 to 44 years in western Washington, we assessed the relationship between carriership of a genetic clotting factor II variant (20210 G-->A) and myocardial infarction (MI). The factor II variant was previously shown to be present in 1% to 2% of the population, to increase the levels of factor II, and to be associated with venous thrombotic disease. Personal interviews and blood samples were obtained from 79 women with a first myocardial infarction and 381 control women identified through random-digit telephone dialing. Polymerase chain reaction (PCR) method was used to determine the factor II **genotypes**. The factor II 20210 G to A transition was present more often in women with MI (5.1%) than among control women (1.6%). The age-adjusted odds ratio for MI was 4.0 (95% confidence interval 1.1 to 15.1). The **relative risk** was high when another major **cardiovascular risk** factor was also present, such as smoking (odds ratio 43.3, 95% confidence interval 6.7 to 281), and the **risk** seemed limited to those with other **risk** factors. These results, in which the effect of major coronary **risk** factors is enhanced fourfold to sixfold by the prothrombin variant, are similar to those previously reported for another genetic clotting abnormality, factor V Leiden. We conclude that factor II 20210 G to A increases the **risk** of myocardial infarction in young women, especially in the women with other major **risk** factors for coronary heart disease.

L2 ANSWER 76 OF 80 MEDLINE on STN
Full Text
AN 1997336683 MEDLINE
DN PubMed ID: 9193430
TI Tissue plasminogen activator and **risk** of myocardial infarction. The Rotterdam Study.
AU van der Bom J G; de Knijff P; Haverkate F; Bots M L; Meijer P; de Jong P T; Hofman A; Kluft C; Grobbee D E
CS Department of Epidemiology and Biostatistics, Erasmus University Medical School, Rotterdam, Netherlands.
SO Circulation, (1997 Jun 17) Vol. 95, No. 12, pp. 2623-7.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199707
ED Entered STN: 24 Jul 1997
Last Updated on STN: 29 Jan 1999
Entered Medline: 17 Jul 1997
AB BACKGROUND: Impaired fibrinolytic capacity, as assessed by euglobulin clot lysis time or plasma concentration of fibrinolytic parameters, has been associated with an increased **risk** of myocardial infarction (MI). We studied the association of a polymorphism in the gene for TPA and of plasma concentrations of TPA (antigen and activity) with the prevalence of MI. METHODS AND RESULTS: A case-control study was performed. Subjects with a history of MI (n = 121) and controls (n = 250) were drawn from the Rotterdam Study, a population-based cohort study of 7983 subjects > or = 55 years old. We determined TPA antigen and activity in plasma and

genotyped all subjects for the Alu repeat insertion/deletion polymorphism in intron h in the TPA gene. Homozygosity for the insertion was associated with twice as many cases of MI as was homozygosity for the deletion (odds ratio, 2.24; 95% CI, 1.11-4.50). TPA antigen was positively associated with the **risk** of MI; compared with that in the lowest quartile, the **relative risks** (odds ratio) in the second, third, and upper quartiles were 1.7 (CI, 0.9-3.3), 2.3 (1.2-4.4), and 2.0 (1.0-3.8), respectively. When adjusted for body mass index, HDL and total cholesterol, systolic and diastolic blood pressures, and current smoking, the **risk** associated with TPA antigen concentration was attenuated. Increased concentrations of TPA activity tended to be associated with an increased **risk** of MI. CONCLUSIONS: This study provides evidence for an independent association of the insertion allele of the insertion/deletion polymorphism in the TPA gene with nonfatal MI. Increased TPA antigen is associated with an increased **risk** of MI; however, this association was not independent of **cardiovascular** disease **risk** factors.

L2 ANSWER 77 OF 80 MEDLINE on STN
Full Text
AN 1997027514 MEDLINE
DN PubMed ID: 8873653
TI Genetic polymorphism of methylenetetrahydrofolate reductase and myocardial infarction. A case-control study.
AU Schmitz C; Lindpaintner K; Verhoef P; Gaziano J M; Buring J
CS Division of Cardiovascular Diseases, Brigham and Women's Hospital, Boston, MA 02115, USA.
NC K04-HL-03138-01 (United States NHLBI)
SO Circulation, (1996 Oct 15) Vol. 94, No. 8, pp. 1812-4.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199612
ED Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
Entered Medline: 16 Dec 1996
AB BACKGROUND: Elevated total plasma homocyst(e)ine (tHcy; the composite of homocysteine-derived moieties in their oxidized and reduced forms) levels are a **risk** factor for coronary heart disease, stroke, and venous thrombosis. tHcy plasma levels are influenced by folate, vitamins B6 and B12, as well as by hereditary factors. A point mutation (C677T) in the gene encoding methylenetetrahydrofolate reductase, an enzyme involved in homocysteine remethylation, has been reported to render the enzyme thermolabile and less active and has been associated with elevated tHcy in homozygous carriers (+/+ **genotype**) as well as with increased **risk** of premature **cardiovascular** disease. METHODS AND RESULTS: We investigated whether this mutation influences **risk** for myocardial infarction (MI) and plasma levels of tHcy and whether this effect may be modified by dietary folate intake in 190 MI cases and 188 control subjects from the Boston Area Health Study. **Genotype** frequencies were 37.8% for -/-, 47.8% for +/-, and 14.4% for +/+ in the control group and 50.0% for -/-, 34.7% for +/-, and 15.3% for +/+ in the case group. The **relative risk** for MI associated with the +/+ **genotype** (compared with +/- and -/-) was 1.1 (95% CI, 0.6 to 1.9; P = .8). Stratification by folate intake values above and below the median did not significantly alter these results. Plasma tHcy levels were 9.9 +/- 2.7 mumol/L in -/- individuals, 10.6 +/- 3.8 mumol/L in +/- individuals, and 9.1 +/- 2.3 mumol/L in +/+ individuals (Ptrend = NS; determined in 68 cases and 59 control subjects). CONCLUSIONS: Our data show that homozygosity for the C677T mutation in this largely white, middle-class US population is not associated with increased **risk** for MI, irrespective of folate intake. This suggests that this mutation does not represent a useful marker for increased **cardiovascular risk** in this and in similar populations.

L2 ANSWER 78 OF 80 MEDLINE on STN
Full Text
AN 1996177833 MEDLINE
DN PubMed ID: 8598840
TI Absence of association or genetic linkage between the

angiotensin-converting-enzyme gene and left ventricular mass.
AU Lindpaintner K; Lee M; Larson M G; Rao V S; Pfeffer M A; Ordovas J M; Schaefer E J; Wilson A F; Wilson P W; Vasan R S; Myers R H; Levy D
CS Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA.
NC K04-HL03138-01 (United States NHLBI)
N01-38038
RR03655 (United States NCRR)
SO The New England journal of medicine, (1996 Apr 18) Vol. 334, No. 16, pp. 1023-8.
Journal code: 0255562. ISSN: 0028-4793.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199604
ED Entered STN: 6 May 1996
Last Updated on STN: 6 Feb 1998
Entered Medline: 25 Apr 1996
AB BACKGROUND. Homozygous carries of the D allele of the angiotensin-converting-enzyme (ACE) gene have been reported to be at increased **risk** for various **cardiovascular** disorders, including left ventricular hypertrophy. We investigated the potential role of the ACE gene in influencing left ventricular mass. METHODS. Quantitative echocardiographic data and DNA samples were available for 2439 subjects from the Framingham Heart Study. ACE **genotypes** were determined by an assay based on the polymerase chain reaction. (The D allele of the ACE gene contains a deletion, whereas the I [insertion] allele does not.) Left ventricular mass and the prevalence of left ventricular hypertrophy, adjusted for clinical covariates, were analyzed according to **genotype**. Genetic linkage between the ACE locus and left ventricular mass was evaluated by quantitative analysis of pairs of siblings. RESULTS. The ACE **genotype** was associated neither with left ventricular mass nor with the prevalence of left ventricular hypertrophy. Mean (+/-SE) left ventricular mass (adjusted for sex) among subjects carrying the DD, DI, and II **genotypes** was 165+/-1.6, 165+/-1.3, and 166+/-2.0 g, respectively (P=0.90). The prevalence of left ventricular hypertrophy among the three **genotype** groups was 15.6 percent, 13.6 percent, and 15.6 percent, respectively (P=0.36), and the adjusted **relative risk** of left ventricular hypertrophy associated with the DD **genotype** was 1.10 (95 percent confidence interval, 0.86 to 1.19). Linkage analysis in 759 pairs of siblings using both the ACE D/I marker and a microsatellite polymorphism at the neighboring locus for the human growth hormone gene failed to support any role of ACE in influencing left ventricular mass. CONCLUSIONS. The ACE **genotype** showed no association with echocardiographically determined left ventricular mass, nor did it confer an increased **risk** of left ventricular hypertrophy. We found no appreciable role of the ACE gene in influencing left ventricular mass.

L2 ANSWER 79 OF 80 MEDLINE on STN
Full Text
AN 1996026113 MEDLINE
DN PubMed ID: 7485169
TI Evidence for a major gene influencing 7-year increases in diastolic blood pressure with age.
AU Cheng L S; Carmelli D; Hunt S C; Williams R R
CS Health Sciences Program, SRI International, Menlo Park, CA 94025-3493, USA.
NC HL21088 (United States NHLBI)
HL24855 (United States NHLBI)
HL50679 (United States NHLBI)
+
SO American journal of human genetics, (1995 Nov) Vol. 57, No. 5, pp. 1169-77.
Journal code: 0370475. ISSN: 0002-9297.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 199511

ED Entered STN: 24 Jan 1996
Last Updated on STN: 24 Jan 1996
Entered Medline: 30 Nov 1995
AB The contribution of genetic factors to blood pressure levels is well established. The contribution of genes to the longitudinal change in blood pressure has been less well studied, because of the lack of longitudinal family data. The present study investigated a possible major-gene effect on the observed increase with age in diastolic blood pressure (DBP) levels. Subjects included 965 unmedicated adults (age > or = 18 years) in 73 pedigrees collected in Utah as part of a longitudinal **cardiovascular** family study. Segregation analysis of DBP change over 7.2 years of follow-up identified a recessive major-gene effect with a gene frequency of p = .23. There was also a significant age effect on the **genotypic** means, which decreased expression of the major gene at older ages. For those inferred to have the **genotype** responsible for large DBP increases, DBP increased 32.3%, compared with a 1.5% increase in the nonsusceptible group (P < .0001). The **relative risk** of developing hypertension between the susceptible and nonsusceptible groups after 7.2 years was 2.4 (P = .006). Baseline DBP reactivities to mental arithmetic (P < .0001), and isometric handgrip (P < .0001) stress tests were greatest in those assigned to the susceptible **genotype.** We conclude that age-related changes in DBP are influenced by a major gene. Characteristics of this major-gene effect for greater age-related blood pressure increases include greater reactivity to mental and physical stressors. The present study thus provides evidence for genetic control of changes in blood pressure, in addition to the previously suggested genetic control of absolute blood pressure level.

L2 ANSWER 80 OF 80 MEDLINE on STN
Full Text
AN 1994224801 MEDLINE
DN PubMed ID: 8170965
TI Insertion/deletion polymorphism of the angiotensin-converting enzyme gene is strongly associated with coronary heart disease in non-insulin-dependent diabetes mellitus.
AU Ruiz J; Blanche H; Cohen N; Velho G; Cambien F; Cohen D; Passa P; Froguel P
CS Centre d'Etude du Polymorphisme Humain, (Fondation Jean Dausset-CEPH), Paris, France.
SO Proceedings of the National Academy of Sciences of the United States of America, (1994 Apr 26) Vol. 91, No. 9, pp. 3662-5.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 13 Jun 1994
Last Updated on STN: 13 Jun 1994
Entered Medline: 1 Jun 1994
AB Non-insulin-dependent diabetes mellitus (NIDDM) is considered a model of premature atherosclerosis with a strong genetic component. We have investigated the role of angiotensin-converting enzyme (ACE; EC 3.4.15.1) gene in 316 unrelated NIDDM individuals, 132 who had myocardial infarction or significant coronary stenoses and 184 with no history of coronary heart disease (CHD). A deletion-polymorphism in the ACE gene was recently reported to be associated with myocardial infarction especially in people classified as low **risk.** Here we report that the D allele of the ACE gene is a strong and independent **risk** factor for CHD in NIDDM patients. The D allele is associated with early-onset CHD in NIDDM, independently of hypertension and lipid values. A progressively increasing **relative risk** in individuals heterozygous and homozygous for the D allele was observed (odds ratios of 1.41 and 2.35, respectively; P < 0.007), suggesting a codominant effect on the **cardiovascular risk.** The percentage of CHD attributable to the ACE deletion allele was 24% in this NIDDM population. Identification of NIDDM patients carrying this putative CHD-susceptibility **genotype** would help early detection and treatment of CHD.

=> s l2 and (SNP or polymorphism)

```
         12044 SNP
          9723 SNPS
         16973 SNP
                (SNP OR SNPS)
        139727 POLYMORPHISM
         49100 POLYMORPHISMS
        149422 POLYMORPHISM
                (POLYMORPHISM OR POLYMORPHISMS)
L3          57 L2 AND (SNP OR POLYMORPHISM)

=> d bib ab 1-57

L3   ANSWER 1 OF 57     MEDLINE on STN
Full Text
AN   2008511270     MEDLINE
DN   PubMed ID: 18672474
TI   Interrelationships among the MTHFR 677C>T polymorphism, migraine, and
     cardiovascular disease.
AU   Schurks Markus; Zee Robert Y L; Buring Julie E; Kurth Tobias
CS   Department of Medicine, Division of Preventive Medicine, Brigham and
     Women's Hospital, Boston, MA 02215-1204, USA.
NC   CA-47988 (United States NCI)
     HL-080467 (United States NHLBI)
     HL-43851 (United States NHLBI)
SO   Neurology, (2008 Aug 12) Vol. 71, No. 7, pp. 505-13.  Electronic
     Publication: 2008-07-30.
     Journal code: 0401060. E-ISSN: 1526-632X.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
     (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA   English
FS   Abridged Index Medicus Journals; Priority Journals
EM   200810
ED   Entered STN: 13 Aug 2008
     Last Updated on STN: 15 Oct 2008
     Entered Medline: 14 Oct 2008
AB   BACKGROUND: Interrelationships among the MTHFR 677C>T polymorphism
     (rs1801133), migraine, and cardiovascular disease (CVD) are plausible
     but remain controversial.  METHODS: Association study among 25,001 white
     US women, participating in the Women's Health Study, with information on
     MTHFR 677C>T polymorphism.  Migraine and migraine aura status were
     self-reported.  Incident CVD events were confirmed after medical record
     review.  We used logistic regression to investigate the
     genotype-migraine association and proportional hazards models to
     evaluate the interrelationships of genotype and migraine on incident
     CVD.  RESULTS: At baseline, 4,577 (18.3%) women reported history of
     migraine; 39.5% of the 3,226 women with active migraine indicated aura.
     During a mean of 11.9 years of follow-up, 625 CVD events occurred.
     Carriers of the TT genotype were less likely to have migraine with aura.
     The multivariable-adjusted relative risk (RR) in the recessive model
     was 0.79 (95% CI = 0.65-0.96; p = 0.02).  The TT genotype did not
     increase the risk for CVD.  In contrast, migraine with aura doubled
     the risk for CVD (multivariable-adjusted RR = 2.06; 95% CI =
     1.53-2.78; p < 0.0001).  Coexistence of migraine with aura and the TT
     genotype selectively raised this risk (RR = 3.66; 95% CI = 1.69-7.90;
     p = 0.001).  This pattern was driven by a fourfold increased risk for
     ischemic stroke (multivariable-adjusted RR = 4.19; 95% CI = 1.38-12.74; p
     = 0.01) and was not apparent for myocardial infarction.  CONCLUSIONS: Data
     from this large cohort of women suggest a modest protective effect of the
     MTHFR 677TT genotype on migraine with aura.  The increased risk for
     cardiovascular disease among migraineurs with aura was magnified for TT
     genotype carriers, which was driven by a substantially increased risk
     of ischemic stroke.

L3   ANSWER 2 OF 57     MEDLINE on STN
Full Text
AN   2007502297     MEDLINE
DN   PubMed ID: 17452407
TI   Association between oestrogen receptor alpha gene polymorphism and
     mortality in female end-stage renal disease patients.
AU   Kato Sawako; Lindholm Bengt; Axelsson Jonas; Qureshi Rashid A; Barany
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Peter; Heimburger Olof; Gustafsson Jan-Ake; Stenvinkel Peter; Nordfors Louise
CS Division of Renal Medicine, Department of Clinical Science, Intervention and Technology, Karolinska University Hospital Huddinge, K-56, 141 86, Stockholm, Sweden.
SO Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, (2007 Sep) Vol. 22, No. 9, pp. 2571-7. Electronic Publication: 2007-04-23.
Journal code: 8706402. ISSN: 0931-0509.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200711
ED Entered STN: 29 Aug 2007
Last Updated on STN: 8 Dec 2007
Entered Medline: 30 Nov 2007
AB BACKGROUND: In the general population, genetic variations in the oestrogen receptor alpha (ERalpha) gene may influence lipid abnormalities, **cardiovascular** disease (**CVD**), and mortality, but this has not previously been studied in end-stage renal disease (ESRD) patients. METHODS: A total of 227 ESRD (141 men and 86 women) patients starting renal replacement therapy (RRT) were **genotyped** for three ERalpha gene **polymorphisms** (Ser10Ser, PvuII and XbaI) and the associations between these **polymorphisms** and clinical and laboratory parameters and survival were analysed. Patients were followed for a median period of 55 months (range 1-126 months). RESULTS: The PvuII and XbaI **polymorphisms** were not associated with any of the clinical parameters. The ERalpha Ser10Ser CC **genotype** was present in 24 (28%) of the female and in 37 (26%) of the male patients. When comparing the CC **genotype** with the CT and TT **genotypes**, there were significant differences in lipid levels and inflammatory marker levels, especially in female patients. In female patients, the CC **genotype** was associated with lower prevalence of protein energy wasting (PEW) (17.4% vs 43.1%; P=0.03), lower median serum triglyceride (1.7 vs 2.1 mmol/l; P=0.001), higher median serum albumin (34.0 vs 32.5 g/l; P=0.03) and lower median high sensitivity-CRP (hsCRP) (2.2 vs 5.5 mg/l; P=0.03) levels compared with the CT plus TT **genotypes**. In male patients only HDL-cholesterol and ApoA levels were associated with this **polymorphism**. Whereas this **polymorphism** did not influence survival in males, the mortality was lower in female patients with the CC **genotype** (Kaplan-Meier; Log-rank 2.2, P=0.02). Moreover, female patients with the CT plus TT **genotypes** had a borderline significant increased **relative risk** (Cox hazard model; 6.6, 95% CI: 0.87-49.9 P=0.06) of death as compared with those with the CC **genotype**, even after adjustment for age and prevalence of **CVD**. CONCLUSIONS: Female, but not male ESRD patients with the ERalpha Ser10Ser CC **genotype** had lower prevalence of PEW, lower serum triglyceride, higher serum albumin and lower hsCRP levels. As this **genotype** was associated with a significantly decreased **risk** of all-cause death during the initial years of RRT, its protective properties need further study.

L3 ANSWER 3 OF 57 MEDLINE on STN
Full Text
AN 2007493117 MEDLINE
DN PubMed ID: 17712123
TI Single nucleotide **polymorphisms** at the adiponectin locus and **risk** of coronary heart disease in men and women.
AU Pischon Tobias; Pai Jennifer K; Manson JoAnn E; Hu Frank B; Rexrode Kathryn M; Hunter David; Rimm Eric B
CS Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts, USA.. pischon@mail.dife.de
NC CA55075 (United States NCI)
HL34594 (United States NHLBI)
HL35464 (United States NHLBI)
SO Obesity (Silver Spring, Md.), (2007 Aug) Vol. 15, No. 8, pp. 2051-60.
Journal code: 101264860. ISSN: 1930-7381.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LA English
FS Priority Journals
EM 200711
ED Entered STN: 23 Aug 2007
Last Updated on STN: 4 Nov 2007
Entered Medline: 2 Nov 2007
AB OBJECTIVE: The objective was to examine the association of 5 common single nucleotide **polymorphisms** (**SNPs**) at the adiponectin locus with **risk** of coronary heart disease (CHD) in men and women. METHODS AND PROCEDURES: We **genotyped** five common **SNPs** in the adiponectin gene (rs266729, -11365C>G; rs822395, -4034A>C; rs822396, -3964A>G; rs2241766, +45T>G; and rs1501299, +276G>T) in men (Health Professionals Follow-up Study) and women (Nurses' Health Study) in a nested case control setting. Among participants free of **cardiovascular** disease at baseline, 266 men and 249 women developed non-fatal myocardial infarction or fatal CHD during 6 and 8 years of follow-up, respectively. In addition, 564 men had coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty. Using **risk** set sampling, controls were selected 2:1 matched on age, smoking, and date of blood draw. RESULTS: The -4034CC **genotype** was related to an increased **risk** of non-fatal myocardial infarction or fatal CHD compared with the AA **genotype** [**relative risk** (RR), men, 1.69; 95% confidence interval (CI), 0.99 to 2.89; women, 2.04; 95% CI, 1.20 to 3.49); however, this **genotype** was not related to **risk** of coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty or to plasma adiponectin levels. Other **SNPs** or haplotypes defined by the 5 **SNPs** were not consistently related to **risk** of CHD in men and women or to plasma adiponectin levels. DISCUSSION: Our study does not support the hypothesis that these 5 common **SNPs** in the adiponectin gene play an important role in the development of CHD among men and women, although we cannot exclude an association between the -4034CC **genotype** and **risk** of CHD.

L3 ANSWER 4 OF 57 MEDLINE on STN
Full Text
AN 2007491720 MEDLINE
DN PubMed ID: 17622934
TI The endothelial nitric oxide synthase gene -786T/C **polymorphism** is a predictive factor for reattacks of coronary spasm.
AU Nishijima Tsunenori; Nakayama Masafumi; Yoshimura Michihiro; Abe Koji; Yamamuro Megumi; Suzuki Satoru; Shono Makoto; Sugiyama Seigo; Saito Yoshihiko; Miyamoto Yoshihiro; Nakao Kazuwa; Yasue Hirofumi; Ogawa Hisao
CS The Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan.
SO Pharmacogenetics and genomics, (2007 Aug) Vol. 17, No. 8, pp. 581-7. Journal code: 101231005. ISSN: 1744-6872.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200709
ED Entered STN: 23 Aug 2007
Last Updated on STN: 20 Sep 2007
Entered Medline: 19 Sep 2007
AB OBJECTIVE: We previously found a -786T/C **polymorphism** in the 5'-flanking region of the endothelial nitric oxide synthase (eNOS) gene and reported that this **polymorphism** is strongly associated with coronary spasm. In this study, we examined whether the **polymorphism** is a prognostic marker in coronary spasm patients. METHODS AND RESULTS: We examined the clinical courses of 201 consecutive patients with coronary spasm who were admitted to our institution: 146 patients with the -786T/T **genotype**; 50 patients with the -786C/T **genotype**; and five patients with the -786C/C **genotype**. The mean follow-up period was 76+/-60 months. All the patients took calcium channel blockers and/or nitrate during the follow-up period. In this study, no patients died due to a cardiac event. About 25 patients were readmitted owing to **cardiovascular** disease. Out of these 25 patients, 23 patients were readmitted owing to a reattack of coronary spasm. The -786C allele was significantly associated with readmission due to coronary spasm (P=0.0072, odds ratio: 3.37 in the dominant effect). Kaplan-Meier analysis revealed that the occurrence of readmission was significantly higher in the patients with the -786C allele than in the patients without the -786C allele (P=0.0079). Further, multiple logistic regression analysis revealed that the -786T/C **polymorphism** was an

independent predictor for readmission due to reattack of coronary spasm (P=0.006; **relative risk**=3.590). CONCLUSIONS: The eNOS -786C allele is an independent **risk** factor for readmission due to a recurrent attack of coronary spasm in patients with coronary spasm, even if the patients have taken calcium channel blockers and/or nitrate.

L3 ANSWER 5 OF 57 MEDLINE on STN
Full Text
AN 2007391765 MEDLINE
DN PubMed ID: 17577421
TI The impact of the catechol-O-methyltransferase Val158Met **polymorphism** on survival in the general population--the HUNT study.
AU Hagen Knut; Stovner Lars J; Skorpen Frank; Pettersen Elin; Zwart John-Anker
CS Department of Clinical Neuroscience, Faculty of medicine, Norwegian University of Science and Technology, Trondheim, Norway.. knut.hagen@ntnu.no
SO BMC medical genetics, (2007) Vol. 8, pp. 34. Electronic Publication: 2007-06-19.
Journal code: 100968552. E-ISSN: 1471-2350.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200707
ED Entered STN: 6 Jul 2007
Last Updated on STN: 7 Jul 2007
Entered Medline: 6 Jul 2007
AB BACKGROUND: The catechol-O-methyltransferase (COMT) gene contains a functional **polymorphism**, Val158Met which has been related to common diseases like cancer, psychiatric illness and myocardial infarction. Whether the Val158Met **polymorphism** is associated with survival has not been evaluated in the general population. The aim of this prospective study was to evaluate the impact of codon 158 COMT gene **polymorphism** on survival in a population-based cohort. METHODS: The sample comprised 2979 non-diabetic individuals who participated in the Nord-Trondelag Health Study (HUNT) in the period 1995-97. The subjects were followed up with respect to mortality throughout year 2004. RESULTS: 212 men and 183 women died during the follow up. No association between codon 158 COMT gene **polymorphism** and survival was found. The unadjusted **relative risk** of death by non-ischemic heart diseases with Met/Met or Met/Val **genotypes** was 3.27 (95% confidence interval, 1.19-9.00) compared to Val/Val **genotype**. When we adjusted for age, gender, smoking, coffee intake and body mass index the **relative risk** decreased to 2.89 (95% confidence interval, 1.04-8.00). CONCLUSION: During 10 year of follow-up, the Val158Met **polymorphism** had no impact on survival in a general population. Difference in mortality rates from non-ischemic heart diseases may be incidental and should be evaluated in other studies.

L3 ANSWER 6 OF 57 MEDLINE on STN
Full Text
AN 2007204997 MEDLINE
DN PubMed ID: 16702981
TI Antihypertensive therapy, the alpha-adducin **polymorphism**, and **cardiovascular** disease in high-**risk** hypertensive persons: the Genetics of Hypertension-Associated Treatment Study.
AU Davis B R; Arnett D K; Boerwinkle E; Ford C E; Leiendecker-Foster C; Miller M B; Black H; Eckfeldt J H
CS School of Public Health, University of Texas-Houston, Houston, TX 77030, USA.. barry.r.davis@uth.tmc.edu
SO The pharmacogenomics journal, (2007 Apr) Vol. 7, No. 2, pp. 112-22. Electronic Publication: 2006-05-16.
Journal code: 101083949. ISSN: 1470-269X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(CLINICAL TRIAL)
LA English
FS Priority Journals
EM 200706
ED Entered STN: 6 Apr 2007
Last Updated on STN: 21 Jun 2007

Entered Medline: 20 Jun 2007

AB In a double-blind, outcome trial conducted in hypertensive patients randomized to chlorthalidone (C), amlodipine (A), lisinopril (L), or doxazosin (D), the alpha-adducin Gly460Trp **polymorphism** was typed (n=36 913). Mean follow-up was 4.9 years. **Relative risks** (RRs) of chlorthalidone versus other treatments were compared between **genotypes** (Gly/Gly+Gly/Trp versus Trp/Trp). Primary outcome was coronary heart disease (CHD). Coronary heart disease incidence did not differ among treatments or **genotypes** nor was there any interaction between treatment and **genotype** (P=0.660). Subgroup analyses indicated that Trp allele carriers had greater CHD **risk** with C versus A+L in women (RR=1.31) but not men (RR=0.91) with no RR gender differences for non-carriers (gender-gene-treatment interaction, P=0.002). The alpha-adducin gene is not an important modifier of antihypertensive treatment on **cardiovascular risk**, but women Trp allele carriers may have increased CHD **risk** if treated with C versus A or L. This must be confirmed to have implications for hypertension treatment.

L3 ANSWER 7 OF 57 MEDLINE on STN

Full Text

AN 2007061002 MEDLINE

DN PubMed ID: 17198546

TI **Risk** factors and myocardial infarction in patients with obstructive sleep apnea: impact of beta2-adrenergic receptor **polymorphisms.**

AU Bartels Nina K; Borgel Jan; Wieczorek Stefan; Buchner Nikolaus; Hanefeld Christoph; Bulut Daniel; Mugge Andreas; Rump Lars C; Sanner Bernd M; Epplen Jorg T

CS Human Genetics, Ruhr-University Bochum, Germany.. the.sirius@web.de

SO BMC medicine, (2007) Vol. 5, pp. 1. Electronic Publication: 2007-01-01. Journal code: 101190723. E-ISSN: 1741-7015.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LA English

FS Priority Journals

EM 200703

ED Entered STN: 2 Feb 2007
Last Updated on STN: 14 Mar 2007
Entered Medline: 13 Mar 2007

AB BACKGROUND: The increased sympathetic nervous activity in patients with obstructive sleep apnea (OSA) is largely responsible for the high prevalence of arterial hypertension, and it is suggested to adversely affect triglyceride and high-density lipoprotein (HDL) cholesterol levels in these patients. The functionally relevant **polymorphisms** of the beta2-adrenergic receptor (Arg-47Cys/Arg16Gly and Gln27Glu) have been shown to exert modifying effects on these **risk** factors in previous studies, but results are inconsistent. METHODS: We investigated a group of 429 patients (55 +/- 10.7 years; 361 men, 68 women) with moderate to severe obstructive sleep apnea (apnea/hypopnea index (AHI) 29.1 +/- 23.1/h) and, on average, a high **cardiovascular risk** profile (body mass index 31.1 +/- 5.6, with hypertension in 60.1%, dyslipidemia in 49.2%, and diabetes in 17.2% of patients). We typed the beta2-adrenergic receptor **polymorphisms** and investigated the five most frequent haplotypes for their modifying effects on OSA-induced changes in blood pressure, heart rate, and lipid levels. The prevalence of **cardiovascular risk** factors and coronary heart disease (n = 55, 12.8%) and survived myocardial infarction (n = 27, 6.3%) were compared between the **genotypes** and haplotypes. RESULTS: Multivariate linear/logistic regressions revealed a significant and independent (from BMI, age, sex, presence of diabetes, use of antidiabetic, lipid-lowering, and antihypertensive medication) influence of AHI on daytime systolic and diastolic blood pressure, heart rate, prevalence of hypertension, and triglyceride and HDL levels. The beta2-adrenergic receptor **genotypes** and haplotypes showed no modifying effects on these relationships or on the prevalence of dyslipidemia, diabetes, and coronary heart disease, yet, for all three **polymorphisms**, heterozygous carriers had a significantly lower **relative risk** for myocardial infarction (Arg-47Cys: n = 195, odds ratio (OR) = 0.32, P = 0.012; Arg16Gly: n = 197, OR = 0.39, P = 0.031; Gln27Glu: OR = 0.37, P = 0.023). Carriers of the most frequent haplotype (n = 113) (haplotype 1; heterozygous for all three **polymorphisms**) showed a five-fold lower prevalence of survived myocardial infarction (OR = 0.21, P = 0.023). CONCLUSION: Our study showed no significant modifying effect of the

functionally relevant beta2-adrenergic receptor **polymorphisms** on OSA-induced blood pressure, heart rate, or lipid changes. Nevertheless, heterozygosity of these **polymorphisms** is associated with a lower prevalence of survived myocardial infarction in this group with, on average, a high **cardiovascular risk** profile.

L3 ANSWER 8 OF 57 MEDLINE on STN
Full Text
AN 2007005509 MEDLINE
DN PubMed ID: 17174637
TI Absence of an interaction between the angiotensin-converting enzyme insertion-deletion **polymorphism** and pravastatin on **cardiovascular** disease in high-**risk** hypertensive patients: the Genetics of Hypertension-Associated Treatment (GenHAT) study.
AU Maitland-van der Zee Anke-Hilse; Boerwinkle Eric; Arnett Donna K; Davis Barry R; Leiendecker-Foster Catherine; Miller Michael B; Klungel Olaf H; Ford Charles E; Eckfeldt John H
CS School of Public Health, University of Texas Health Science Center at Houston, 1200 Hermann Pressler, Houston TX, USA.. a.h.maitland@pharm.uu.nl
SO American heart journal, (2007 Jan) Vol. 153, No. 1, pp. 54-8.
Journal code: 0370465. E-ISSN: 1097-6744.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200701
ED Entered STN: 5 Jan 2007
Last Updated on STN: 26 Jan 2007
Entered Medline: 25 Jan 2007
AB BACKGROUND: The aim of this study was to determine whether the angiotensin-converting enzyme (ACE) insertion-deletion (ID) **polymorphism** interacts with pravastatin to modify the **risk** of coronary heart disease (CHD) and other **cardiovascular** end points in a large clinical trial. METHODS: GenHAT is an ancillary study of the ALLHAT. The ACE ID **genotyped** population in the lipid-lowering arm of ALLHAT included 9467 participants randomly assigned to pravastatin (n = 4741) or to usual care (n = 4726). The efficacy of pravastatin in reducing the **risk** of primary outcome (all-cause mortality) and secondary outcomes (fatal CHD and nonfatal myocardial infarction, **cardiovascular** disease [**CVD**] mortality, CHD, stroke, other **CVD**, non-**CVD** mortality, stroke, and heart failure) was compared between the **genotype** strata (dominant model ID + II vs DD, additive model II vs ID vs DD), by examining an interaction term in a Cox proportional hazards model. RESULTS: The **relative risk** of fatal CHD and nonfatal myocardial infarction among subjects randomized to pravastatin compared with subjects randomized to usual care was similar in subjects with the II **genotype** (hazard ratio [HR] 0.84, 95% CI 0.59-1.18), the ID **genotype** (HR 0.84, 95% CI 0.68-1.03), and the DD **genotype** (HR 0.99, 95% CI 0.77-1.27). CONCLUSIONS: We found no evidence that the ACE ID **genotype** was a major modifier of the efficacy of pravastatin in reducing the **risk** of **cardiovascular** events.

L3 ANSWER 9 OF 57 MEDLINE on STN
Full Text
AN 2006639796 MEDLINE
DN PubMed ID: 17023672
TI TGF-beta 1 **polymorphisms** and **risk** of myocardial infarction and stroke: the Rotterdam Study.
AU Sie Mark P S; Uitterlinden Andre G; Bos Michiel J; Arp Pascal P; Breteler Monique M B; Koudstaal Peter J; Pols Huibert A P; Hofman Albert; van Duijn Cornelia M; Witteman Jacqueline C M
CS Department of Epidemiology and Biostatistics, Erasmus Medical Center, Rotterdam, PO Box 2040, 3000 CA Rotterdam, The Netherlands.
SO Stroke; a journal of cerebral circulation, (2006 Nov) Vol. 37, No. 11, pp. 2667-71. Electronic Publication: 2006-10-05.
Journal code: 0235266. E-ISSN: 1524-4628.
CY United States
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200611

ED Entered STN: 1 Nov 2006
Last Updated on STN: 15 Nov 2006
Entered Medline: 14 Nov 2006
AB BACKGROUND AND PURPOSE: Inflammation plays a pivotal role in the pathogenesis of atherosclerosis and of **cardiovascular** and cerebrovascular complications. Transforming growth factor-beta1 (TGF-beta1) is a pleiotropic cytokine with a central role in inflammation. Little is known of the relation of variations within the gene and **risk** of **cardiovascular** and cerebrovascular disease. We therefore investigated 5 **polymorphisms** in the TGF-beta1 gene (-800 G/A, -509 C/T, codon 10 Leu/Pro, codon 25 Arg/Pro, and codon 263 Thr/Ile) in relation to the **risk** of myocardial infarction and stroke in a population-based study. METHODS: Participants (N=6456) of the Rotterdam Study were included in the current study. Analyses of the relations of **genotypes** with the **risk** of myocardial infarction and stroke were performed according to Cox proportional-hazards methods. All analyses were adjusted for age, sex, conventional **cardiovascular risk** factors, and medical history. RESULTS: We found no association with the **risk** of myocardial infarction. A significantly increased **risk** of stroke was found, associated with the T allele of the -509 C/T **polymorphism** (**relative risk**, 1.26; (95% CI, 1.06 to 1.49) and the Pro variant of the codon 10 **polymorphism** (**relative risk**, 1.24; 95% CI, 1.04 to 1.48). CONCLUSIONS: No association between the TGF-beta1 **polymorphisms** and myocardial infarction was observed; however, the -509 C/T and codon 10 Leu/Pro **polymorphisms** were associated with the **risk** of stroke.

L3 ANSWER 10 OF 57 MEDLINE on STN
Full Text
AN 2006596240 MEDLINE
DN PubMed ID: 16849409
TI A functional **polymorphism** in the glucocorticoid receptor gene and its relation to **cardiovascular** disease **risk** in familial hypercholesterolemia.
AU Koeijvoets Kristel C M C; van Rossum Elisabeth F C; Dallinga-Thie Geesje M; Steyerberg Ewout W; Defesche Joep C; Kastelein John J P; Lamberts Steven W J; Sijbrands Eric J G
CS Department of Internal Medicine, D435, Erasmus Medical Center, P.O. Box 2040, 3000 AC Rotterdam, The Netherlands.
SO The Journal of clinical endocrinology and metabolism, (2006 Oct) Vol. 91, No. 10, pp. 4131-6. Electronic Publication: 2006-07-18.
Journal code: 0375362. ISSN: 0021-972X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200611
ED Entered STN: 11 Oct 2006
Last Updated on STN: 14 Nov 2006
Entered Medline: 13 Nov 2006
AB CONTEXT: Individuals with the functional ER22/23EK variant in the glucocorticoid receptor gene are relatively resistant to the downstream consequences of glucocorticoids. Evidence suggests that carriers have a more favorable **cardiovascular risk** profile, but the relationship between this ER22/23EK variant and **cardiovascular** disease has not been hitherto assessed. OBJECTIVE: We, therefore, determined whether carriership of the ER22/23EK improves **cardiovascular** disease **risk** in patients with severe hypercholesterolemia. DESIGN, SETTING, AND PARTICIPANTS: In a multicenter cohort study, 2024 patients with heterozygous familial hypercholesterolemia, aged 18 yr and older, were **genotyped** for the ER22/23EK **polymorphism**. Patients were identified at lipid clinics throughout The Netherlands between 1989 and 2002. MAIN OUTCOME MEASURES: The primary outcome measure was **cardiovascular** disease. RESULTS: Seventy-six (7.8%) of 977 men and 72 (6.9%) of 1047 women were carriers of the ER22/23EK variant. A total of 395 men and 247 women had a **cardiovascular** event. In contrast to expected results, we observed no significant association of the ER22/23EK variant with **cardiovascular** disease **risk** (men: **relative risk**, 0.75; 95% confidence interval, 0.50-1.14; P = 0.2; women: **relative risk**, 1.37; 95% confidence interval, 0.82-2.28; P = 0.2). However, we found a significant interaction between gender and the **polymorphism** on **cardiovascular** disease (P = 0.02). CONCLUSIONS: In this large cohort of individuals with very high **risk** of **cardiovascular** disease, the association between the functional ER22/23EK **polymorphism** and

cardiovascular risk was not significant overall, although it varied significantly by gender.

L3 ANSWER 11 OF 57 MEDLINE on STN
Full Text
AN 2006237048 MEDLINE
DN PubMed ID: 16645019
TI An insulin-like growth factor-I gene **polymorphism** modifies the **risk** of microalbuminuria in subjects with an abnormal glucose tolerance.
AU Rietveld I; Hofman A; Pols H A P; van Duijn C M; Lamberts S W J; Janssen J A M J L
CS Department of Internal Medicine, Rotterdam, The Netherlands.
SO European journal of endocrinology / European Federation of Endocrine Societies, (2006 May) Vol. 154, No. 5, pp. 715-21.
Journal code: 9423848. ISSN: 0804-4643.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200606
ED Entered STN: 29 Apr 2006
Last Updated on STN: 30 Jun 2006
Entered Medline: 29 Jun 2006
AB OBJECTIVE: Microalbuminuria (MA) is related to **cardiovascular** disease both in diabetic patients and non-diabetic subjects. DESIGN: We investigated whether a **polymorphism** near the promoter region of the IGF-I gene was related to the development of MA. METHODS: For this study, 1069 participants of the Rotterdam study were selected (440 participants with an abnormal glucose tolerance (AGT), 220 participants with type 2 diabetes and 254 subjects with pre-diabetes, and 595 subjects with a normal glucose tolerance (NGT). RESULTS: 787 subjects were carriers of the wild type IGF-I **genotype** (73.6%) and 282 subjects were variant carriers (26.4%) of this IGF-I gene **polymorphism**. Compared to subjects with NGT the **risk** for microalbuminuria was higher (Odds Ratio (OR): 3.1 (95% CI: 1.2-7.7); P = 0.02) in variant carriers with AGT than in carriers of the wild type of this IGF-I gene **polymorphism** (OR: 2.2 (95% CI: 1.2-4.0); P = 0.009). Compared with wild type carriers with AGT, the **relative risk** for MA was unadjusted and non-significantly increased in variant carriers with AGT (1.6; 95% CI: 0.8-2.9). However, after adjustment for possible confounding factors (age, gender, mean blood pressure, fasting insulin, fasting glucose and smoking) this **risk** became significant (OR: RR 2.1; 95% CI:1.1-4.4; P = 0.04). CONCLUSIONS: In subjects with AGT, a higher **risk** for MA was observed in variant carriers than in carriers of the wild type **genotype** of this IGF-I gene **polymorphism**. Since MA is primarily associated with **cardiovascular** disease in subjects with AGT, our study suggests that variant carriers have a higher **risk** for **cardiovascular** disease than carriers of the wild type when they develop an AGT.

L3 ANSWER 12 OF 57 MEDLINE on STN
Full Text
AN 2006032628 MEDLINE
DN PubMed ID: 16375773
TI Cystathionine beta-synthase T833C/844INS68 **polymorphism**: a family-based study on mentally retarded children.
AU Dutta Samikshan; Sinha Swagata; Chattopadhyay Anindita; Gangopadhyay Prasanta Kumar; Mukhopadhyay Jotideb; Singh Manoranjan; Mukhopadhyay Kanchan
CS Manovikas Biomedical Research and Diagnostic Centre, E,M, Bypass, Kolkata, India.. mikpal2000@yahoo.com
SO Behavioral and brain functions : BBF, (2005) Vol. 1, pp. 25. Electronic Publication: 2005-12-26.
Journal code: 101245751. E-ISSN: 1744-9081.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; PUBMED-NOT-MEDLINE
EM 200707
ED Entered STN: 20 Jan 2006
Last Updated on STN: 12 Dec 2006
Entered Medline: 24 Jul 2007

AB BACKGROUND: Cystathionine beta-synthase (CBS) mediates conversion of homocysteine to cystathionine and deficiency in enzyme activity may lead to hyperhomocysteinemia/homocystinuria, which are often associated with mental retardation (MR). A large number of **polymorphisms** have been reported in the CBS gene, some of which impair its activity and among these, a T833C **polymorphism** in cis with a 68 bp insertion at 844 in the exon 8 is found to be associated with mild hyperhomocysteinemia in different ethnic groups. METHODS: The present study is aimed at investigating the association between T833C/844ins68 **polymorphism** and MR. One hundred and ninety MR cases were recruited after psychometric evaluation. Hundred and thirty-eight control subjects, two hundred and sixty-seven parents of MR probands and thirty **cardiovascular** disorder (**CVD**) patients were included for comparison. Peripheral blood was collected after obtaining informed written consent. The T833C/844ins68 **polymorphism** was investigated by PCR amplification of genomic DNA and restriction fragment length **polymorphism** analysis, followed by statistical analysis. RESULTS: The **genotypic** distribution of the **polymorphism** was within the Hardy-Weinberg equilibrium. A slightly increased **genotypic** frequency was observed in the Indian control population as compared to other Asian populations. Both haplotype-based haplotype **relative risk** analysis and transmission disequilibrium test reveled lack of association of the T833C/844ins68 **polymorphism** with MR; nevertheless, the **relative risk** calculated was higher (>1) and in a limited number of informative MR families, preferential transmission of the double mutant from heterozygous mothers to the MR probands was noticed (chi2 = 4.00, P < 0.05). CONCLUSION: This is the first molecular genetic study of CBS gene dealing with T833C/844ins68 double mutation in MR subjects. Our preliminary data indicate lack of association between T833C/844ins68 **polymorphism** with MR. However, higher **relative risk** and biased transmission of the double mutation from heterozygous mothers to MR probands are indicative of a **risk** of association between this **polymorphism** with mental retardation.

L3 ANSWER 13 OF 57 MEDLINE on STN
Full Text
AN 2005636076 MEDLINE
DN PubMed ID: 16316363
TI Effects of single-nucleotide **polymorphisms** in MTHFR and MTRR on mortality and allograft loss in kidney transplant recipients.
AU Winkelmayer Wolfgang C; Kramar Reinhard; Sunder-Plassmann Gere; Fodinger Manuela
CS Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Boston, MA 02120, USA.. wolfgang@post.harvard.edu
SO Kidney international, (2005 Dec) Vol. 68, No. 6, pp. 2857-62. Journal code: 0323470. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200602
ED Entered STN: 1 Dec 2005
Last Updated on STN: 2 Feb 2006
Entered Medline: 1 Feb 2006
AB BACKGROUND: Plasma total homocysteine (tHcy) is associated with **cardiovascular** outcomes in kidney transplant recipients (KTR). The methylenetetrahydrofolate-reductase (MTHFR) 677C>T **polymorphism**, an important determinant of plasma tHcy concentrations, could therefore constitute an important prognostic marker. METHODS: We prospectively followed 710 KTR over >6 years. The MTHFR677C>T, MTHFR1298A>C, MTHFR1793G>A, and MTRR66A>G **polymorphisms** were analyzed. Demographic, clinical, and transplant-related information was obtained, and patients were followed-up using the Austrian Dialysis and Transplant Registry. Using Cox regression, we established the independent relations of each **genotype** to the **risk** of death from any cause, and/or kidney allograft loss. RESULTS: During a median follow-up of 6.1 years, 154 participants died and 260 kidney allografts were lost. Compared to patients with the MTHFR677CC **genotype**, patients with MTHFR677CT had an adjusted relative mortality **risk** of 1.02 (95%CI 0.70-1.47), and those with MTHFR677TT of 0.98 (95%CI 0.52-1.85). Compared to MTHFR677CC, the **relative risks** of kidney allograft loss were 0.93 (95%CI 0.70-1.23; MTHFR677CT) and 0.78 (95%CI 0.47-1.30; MTHFR677TT), respectively. None of the other

genotypes were associated with the **risks** studied, either. These findings did not depend on whether we controlled for tHcy levels. CONCLUSION: This study does not support the routine use of MTHFR or MTRR **genotyping** for prognostic evaluation or **risk**-stratification in kidney transplant recipients.

L3 ANSWER 14 OF 57 MEDLINE on STN
Full Text
AN 2005544492 MEDLINE
DN PubMed ID: 16198657
TI Impact of CYP2D6 **genotype** on adverse effects during treatment with metoprolol: a prospective clinical study.
AU Fux Richard; Morike Klaus; Prohmer Anne M T; Delabar Ursula; Schwab Matthias; Schaeffeler Elke; Lorenz Gernot; Gleiter Christoph H; Eichelbaum Michel; Kivisto Kari T
CS Abteilung Klinische Pharmakologie, Lehrbereich Allgemeinmedizin der Medizinischen Fakultat, and Koordinierungszentrum Klinische Studien, Universitatsklinikum Tubingen, Tubingen, Germany.
SO Clinical pharmacology and therapeutics, (2005 Oct) Vol. 78, No. 4, pp. 378-87.
Journal code: 0372741. ISSN: 0009-9236.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200511
ED Entered STN: 14 Oct 2005
Last Updated on STN: 3 Nov 2005
Entered Medline: 2 Nov 2005
AB OBJECTIVE: Our objective was to study the impact of the cytochrome P450 (CYP) 2D6 **polymorphism** on the tolerability of metoprolol in a real-life primary care setting. The adverse effects studied comprised effects related to the central nervous system, **cardiovascular** effects, and sexual dysfunction. METHODS: Patients in whom treatment with metoprolol was considered were enrolled into this prospective, 6-week multicenter study. The dosage of metoprolol was determined on an individual basis and could be freely adjusted on clinical grounds. The indication for treatment was hypertension in about 90% of cases. Systolic and diastolic blood pressure, resting heart rate, and plasma metoprolol and alpha-hydroxymetoprolol concentrations were measured. CYP2D6 **genotyping** covered alleles *3 to *10 and *41 and the duplications. Possible adverse effects of metoprolol were systematically assessed over a 6-week period by means of standardized rating scales and questionnaires. RESULTS: The final study population comprised 121 evaluable patients (all white patients); among them, there were 5 ultrarapid metabolizers (UMs) (4.1%), 91 extensive metabolizers (EMs) (75%), 21 intermediate metabolizers (IMs) (17%), and 4 poor metabolizers (PMs) (3.3%). Plasma metoprolol concentrations normalized for the daily dose and metoprolol/alpha-hydroxymetoprolol ratios at steady state were markedly influenced by CYP2D6 **genotype** and displayed a gene-dose effect. The median of the dose-normalized metoprolol concentration was 0.0088 ng/mL, 0.047 ng/mL, 0.34 ng/mL, and 1.34 ng/mL among UMs, EMs, IMs, and PMs, respectively (P<.0001). There was no significant association between CYP2D6 **genotype**-derived phenotype (EMs and UMs combined versus PMs and IMs combined) and adverse effects during treatment with metoprolol. There was a tendency toward a more frequent occurrence of cold extremities in the PM plus IM group as compared with the EM plus UM group (16.0% versus 4.2%, P=.056; **relative risk**, 3.8 [95% confidence interval, 1.03--14.3]). CONCLUSIONS: CYP2D6 **genotype**-derived phenotype was not significantly associated with a propensity for adverse effects to develop during treatment with metoprolol. However, the results concerning tolerability of metoprolol in PMs were inconclusive because of the small number of PMs enrolled.

L3 ANSWER 15 OF 57 MEDLINE on STN
Full Text
AN 2005472081 MEDLINE
DN PubMed ID: 16139102
TI DNA **polymorphisms** in the tyrosine hydroxylase and GNB3 genes:

association with unexpected death from acute myocardial infarction and increased heart weight.
AU Klintschar M; Stiller D; Schwaiger P; Kleiber M
CS Institute of Legal Medicine, Martin Luther University Halle-Wittenberg, Franzosenweg 1, D06112 Halle, Germany.. michael.klintschar@medizin.uni-halle.de
SO Forensic science international, (2005 Oct 29) Vol. 153, No. 2-3, pp. 142-6. Electronic Publication: 2004-11-06.
Journal code: 7902034. ISSN: 0379-0738.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200512
ED Entered STN: 7 Sep 2005
Last Updated on STN: 18 Dec 2005
Entered Medline: 13 Dec 2005
AB Sudden and unexpected death from myocardial infarction (MI) is one of the most commonly observed findings in forensic medicine. To investigate the biochemical and genetic background of this disease we investigated the **genotypes** for two **polymorphisms** associated with hypertension: TH01, a tetrameric microsatellite in the tyrosine hydroxylase gene and the single nucleotide **polymorphism** C825T in the GNB3 gene in 116 sudden deaths from MI (78 males, 38 females) and in a control group of 137 deaths from natural causes other than MI (52 males, 85 females). For TH01 no correlation with the prevalence of MI was found. For C825T, results were different. While for the male individuals allelic frequencies and **genotype** distributions were similar in both groups, T-homozygosity was significantly more common in female fatalities from MI than in the female control group (24% versus 7%; **Relative Risk** 2.29). Nevertheless, neither for TH01 nor for C825T an association with heart weight was found. Thus our results demonstrate that the C825T **polymorphism** may play a role in the development of myocardial infarctions, at least in females. They also demonstrate that the genetic component in complex diseases like MI may depend on the gender of the patients. As the influence of this **polymorphism** on arterial blood pressure appears to be relatively small, and G-proteins are involved in numerous intracellular signal cascades it can be speculated that T-homozygosity at this locus might influence the incidence or mortality of **cardiovascular** disease via hitherto unknown mechanisms.

L3 ANSWER 16 OF 57 MEDLINE on STN
Full Text
AN 2005394958 MEDLINE
DN PubMed ID: 15920035
TI Peroxisome proliferator-activated receptor-gamma2 P12A **polymorphism** and **risk** of coronary heart disease in US men and women.
AU Pischon Tobias; Pai Jennifer K; Manson JoAnn E; Hu Frank B; Rexrode Kathryn M; Hunter David; Rimm Eric B
CS Department of Nutrition and Epidemiology, Harvard School of Public Health, Boston, Mass, USA.. pischon@mail.dife.de
NC CA55075 (United States NCI)
HL07575 (United States NHLBI)
HL34594 (United States NHLBI)
HL35464 (United States NHLBI)
SO Arteriosclerosis, thrombosis, and vascular biology, (2005 Aug) Vol. 25, No. 8, pp. 1654-8. Electronic Publication: 2005-05-26.
Journal code: 9505803. E-ISSN: 1524-4636.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200512
ED Entered STN: 2 Aug 2005
Last Updated on STN: 30 Dec 2005
Entered Medline: 29 Dec 2005
AB OBJECTIVE: Activation of the peroxisome proliferator-activated receptor-gamma (PPARgamma) improves insulin sensitivity and exerts antiatherogenic effects. A common alanine for proline substitution at

codon 12 in the PPARG2 gene is related to lower receptor activity. Studies suggest that the A12 allele is associated with reduced **risk** of type 2 diabetes; however, data on the **risk** of coronary heart disease (CHD) are scarce and controversial. METHODS AND RESULTS: We examined the relationship between PPARG2 P12A and CHD **risk** in women (Nurses' Health Study) and men (Health Professionals Follow-Up Study) in nested case control settings. Among participants free of **cardiovascular** disease at baseline, 249 women and 266 men developed nonfatal myocardial infarction (MI) or fatal CHD during 8 and 6 years of follow-up, respectively. Using **risk**-set sampling, controls were selected 2:1 matched on age, smoking, and date of blood draw. The **relative risk** (RR) of nonfatal MI or fatal CHD of carriers compared with noncarriers of the A12 allele was 1.17 (95% CI, 0.82 to 1.68) among women and 1.44 (95% CI, 1.00 to 2.07) among men (pooled RR, 1.30 [95% CI, 1.00 to 1.67]). We found a significantly increased **risk** associated with the A12 allele among individuals with a body mass index > or =25 kg/m2 (women: RR, 1.88; 95% CI, 1.01 to 3.50; men: RR, 1.55; 95% CI, 0.92 to 2.60; pooled: RR, 1.68; 95% CI, 1.13 to 2.50) but not among those <25 kg/m2 (pooled RR, 0.86; 95% CI, 0.37 to 1.97; P heterogeneity overweight versus nonoverweight 0.16). CONCLUSIONS: These data do not support the hypothesis that the A12 allele is associated with a decreased **risk** of CHD. The potential interaction between PPARG2 P12A, overweight, and increased CHD **risk** needs further evaluation.

L3 ANSWER 17 OF 57 MEDLINE on STN
Full Text
AN 2005331650 MEDLINE
DN PubMed ID: 15967849
TI Pharmacogenetic association of the angiotensin-converting enzyme insertion/deletion **polymorphism** on blood pressure and **cardiovascular** **risk** in relation to antihypertensive treatment: the Genetics of Hypertension-Associated Treatment (GenHAT) study.
AU Arnett Donna K; Davis Barry R; Ford Charles E; Boerwinkle Eric; Leiendecker-Foster Cathie; Miller Michael B; Black Henry; Eckfeldt John H
CS University of Minnesota, Division of Epidemiology, Minneapolis, USA.. arnett@ms.soph.uab.edu
NC 5 R01 HL-63082 (United States NHLBI)
SO Circulation, (2005 Jun 28) Vol. 111, No. 25, pp. 3374-83. Electronic Publication: 2005-06-20.
Journal code: 0147763. E-ISSN: 1524-4539.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
(CLINICAL TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200602
ED Entered STN: 29 Jun 2005
Last Updated on STN: 4 Feb 2006
Entered Medline: 3 Feb 2006
AB BACKGROUND: Previous studies have reported that blood pressure response to antihypertensive medications is influenced by genetic variation in the renin-angiotensin-aldosterone system, but no clinical trails have tested whether the ACE insertion/deletion (I/D) **polymorphism** modifies the association between the type of medication and multiple **cardiovascular** and renal phenotypes. METHODS AND RESULTS: We used a double-blind, active-controlled randomized trial of antihypertensive treatment that included hypertensives > or =55 years of age with > or =1 **risk** factor for **cardiovascular** disease. ACE I/D **genotypes** were determined in 37 939 participants randomized to chlorthalidone, amlodipine, lisinopril, or doxazosin treatments and followed up for 4 to 8 years. Primary outcomes included fatal coronary heart disease (CHD) and/or nonfatal myocardial infarction. Secondary outcomes included stroke, all-cause mortality, combined CHD, and combined **cardiovascular** disease. Fatal and nonfatal CHD occurred in 3096 individuals during follow-up. The hazard rates for fatal and nonfatal CHD and the secondary outcomes were similar across antihypertensive treatments. ACE I/D **genotype** group was not associated with fatal and nonfatal CHD (**relative risk** of DD versus ID and II, 0.99; 95% CI, 0.91 to 1.07) or any secondary outcome. The 6-year hazard rate for fatal and nonfatal CHD in the DD **genotype** group was not

statistically different from the ID and II **genotype** group by type of treatment. No secondary outcome measure was statistically different across antihypertensive treatment and ACE I/D **genotype** strata. CONCLUSIONS: ACE I/D **genotype** group was not a predictor of CHD, nor did it modify the response to antihypertensive treatment. We conclude that the ACE I/D **polymorphism** is not a useful marker to predict antihypertensive treatment response.

L3 ANSWER 18 OF 57 MEDLINE on STN
Full Text
AN 2005323015 MEDLINE
DN PubMed ID: 15856070
TI TaqIB **polymorphism** in CETP gene: the influence on incidence of **cardiovascular** disease in statin-treated patients with familial hypercholesterolemia.
AU Mohrschladt Martina F; van der Sman-de Beer Femke; Hofman Maaike K; van der Krabben Marieke; Westendorp Rudi Gj; Smelt August Hm
CS Department of General Internal Medicine, Leiden University Medical Center, PO Box 9600, 2300 RC Leiden, The Netherlands.
SO European journal of human genetics : EJHG, (2005 Jul) Vol. 13, No. 7, pp. 877-82.
Journal code: 9302235. ISSN: 1018-4813.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200509
ED Entered STN: 24 Jun 2005
Last Updated on STN: 14 Sep 2005
Entered Medline: 13 Sep 2005
AB The effects of TaqI restriction fragment length **polymorphism** of the CETP gene on the occurrence of **cardiovascular** disease (**CVD**) events were investigated in patients with familial hypercholesterolemia (FH). A total of 300 FH patients, of which 116 (39%) had **CVD** at the start of the study, were treated with statins during a mean period of 8.5 years. The distribution of Taq1B **genotypes** was 31% B1B1, 49% B1B2, and 20% B2B2. No differences were found at baseline between the three **genotypes**, except for an association of the B1 allele with lower high-density lipoprotein (HDL)-cholesterol levels (P=0.003). All patients were put on statins within 6-8 weeks after the first visit; about 60% received simvastatin (20-40 mg daily) and 40% either pravastatin (40 mg daily) or atorvastatin (20-40 mg daily). The different statin treatments were similar for all groups. The mean change of plasma HDL-cholesterol, low-density lipoprotein-cholesterol, and triglyceride concentration during statin therapy was similar for the three **genotypes**. During follow-up, new **CVD** events were recorded in 22 (37%) of the B2B2 patients (n=59) and in 67 (28%) of B1 allele carriers (n=241) (P=0.36). The **relative risk** for **CVD** events, after adjustment for age, gender, and **CVD** at intake, was 1.8 (CI: 1.1-3.0) for B2B2 carriers compared to B1 allele carriers. The Taq1B **polymorphism** is a significant predictor of future **CVD** events in statin-treated patients with FH. In spite of similar improvement of the lipoprotein profile during statin therapy, our FH patients with the B2B2 **genotype** may have a higher **CVD risk** in comparison with the B1 allele carriers.

L3 ANSWER 19 OF 57 MEDLINE on STN
Full Text
AN 2005200594 MEDLINE
DN PubMed ID: 15833936
TI E-selectin **genotypes** and **risk** of type 2 diabetes in women.
AU Meigs James B; Hu Frank B; Perhanidis Jessica S; Hunter David; Rifai Nader; Manson Joann E
CS General Medicine Division, Department of Medicine, Massachusetts General Hospital, Boston, MA 02114, USA.. jmeigs@partners.org
NC CA87969 (United States NCI)
DK36798 (United States NIDDK)
DK46519 (United States NIDDK)
DK58845 (United States NIDDK)
SO Obesity research, (2005 Mar) Vol. 13, No. 3, pp. 513-8.
Journal code: 9305691. ISSN: 1071-7323.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200508
ED Entered STN: 19 Apr 2005
Last Updated on STN: 3 Aug 2005
Entered Medline: 2 Aug 2005
AB Endothelial dysfunction increases **risk** for type 2 diabetes. We examined whether variation in the gene for E-selectin (SELE), a biomarker of endothelial dysfunction, was associated with levels of E-selectin or diabetes quantitative traits (including fasting levels of insulin and hemoglobin A(1c)) in 719 nondiabetic participants of the Nurses' Health Study or with **risk** of diabetes in 602 incident (over 10 years of follow-up) cases and 655 control women matched for age, race, and fasting status. Variation in three single nucleotide **polymorphisms** previously associated with **cardiovascular** disease **risk** and having effects on E-selectin function, S128R, G98T, and L554F, was not significantly (p > 0.05) associated with levels of E-selectin or diabetes quantitative traits, or with **risk** of incident diabetes in the primary analysis. Among women with low levels of subclinical inflammation (C-reactive protein levels below the population median), S128R R allele carriers had a diabetes **risk** factor-adjusted **relative risk** of incident diabetes of 1.71 (95% confidence interval, 1.04 to 2.81) relative to those with the SS **genotype**. Apart from an association in this subgroup, we conclude that the E-selectin variants we examined are not important genetic **risk** factors for type 2 diabetes in women.

L3 ANSWER 20 OF 57 MEDLINE on STN
Full Text
AN 2005068552 MEDLINE
DN PubMed ID: 15640973
TI Association between the gene encoding 5-lipoxygenase-activating protein and stroke replicated in a Scottish population.
AU Helgadottir A; Gretarsdottir S; St Clair D; Manolescu A; Cheung J; Thorleifsson G; Pasdar A; Grant S F A; Whalley L J; Hakonarson H; Thorsteinsdottir U; Kong A; Gulcher J; Stefansson K; MacLeod M J
CS deCODE Genetics, Reykjavik, Iceland.
SO American journal of human genetics, (2005 Mar) Vol. 76, No. 3, pp. 505-9. Electronic Publication: 2005-01-07.
Journal code: 0370475. ISSN: 0002-9297.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS OMIM-603700
EM 200503
ED Entered STN: 9 Feb 2005
Last Updated on STN: 29 Mar 2005
Entered Medline: 28 Mar 2005
AB **Cardiovascular** diseases, including myocardial infarction (MI) and stroke, most often occur on the background of atherosclerosis, a condition attributed to the interactions between multiple genetic and environmental **risk** factors. We recently reported a linkage and association study of MI and stroke that yielded a genetic variant, HapA, in the gene encoding 5-lipoxygenase-activating protein (ALOX5AP), that associates with both diseases in Iceland. We also described another ALOX5AP variant, HapB, that associates with MI in England. To further assess the contribution of the ALOX5AP variants to **cardiovascular** diseases in a population outside Iceland, we **genotyped** seven single-nucleotide **polymorphisms** that define both HapA and HapB from 450 patients with ischemic stroke and 710 controls from Aberdeenshire, Scotland. The Icelandic at-**risk** haplotype, HapA, had significantly greater frequency in Scottish patients than in controls. The carrier frequency in patients and controls was 33.4% and 26.4%, respectively, which resulted in a **relative risk** of 1.36, under the assumption of a multiplicative model (P=.007). We did not detect association between HapB and ischemic stroke in the Scottish cohort. However, we observed that HapB was overrepresented in male patients. This replication of haplotype association with stroke in a population outside Iceland further supports a role for ALOX5AP in **cardiovascular** diseases.

L3 ANSWER 21 OF 57 MEDLINE on STN
Full Text
AN 2005006402 MEDLINE
DN PubMed ID: 15632091
TI Identification of polymorphic motifs using probabilistic search algorithms.
AU Basu Analabha; Chaudhuri Probal; Majumder Partha P
CS Human Genetics Unit, Indian Statistical Institute, Kolkata, 700108 India.
SO Genome research, (2005 Jan) Vol. 15, No. 1, pp. 67-77.
Journal code: 9518021. ISSN: 1088-9051.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200504
ED Entered STN: 6 Jan 2005
Last Updated on STN: 15 Apr 2005
Entered Medline: 14 Apr 2005
AB The problem of identifying motifs comprising nucleotides at a set of polymorphic DNA sites, not necessarily contiguous, arises in many human genetic problems. However, when the sites are not contiguous, no efficient algorithm exists for polymorphic motif identification. A search based on complete enumeration is computationally inefficient. We have developed probabilistic search algorithms to discover motifs of known or unknown lengths. We have developed statistical tests of significance for assessing a motif discovery, and a statistical criterion for simultaneously estimating motif length and discovering it. We have tested these algorithms on various synthetic data sets and have shown that they are very efficient, in the sense that the "true" motifs can be detected in the vast majority of replications and in a small number of iterations. Additionally, we have applied them to some real data sets and have shown that they are able to identify known motifs. In certain applications, it is pertinent to find motifs that contain contrasting nucleotides at the sites included in the motif (e.g., motifs identified in case-control association studies). For this, we have suggested appropriate modifications. Using simulations, we have discovered that the success rate of identification of the correct motif is high in case-control studies except when **relative risks** are small. Our analyses of evolutionary data sets resulted in the identification of some motifs that appear to have important implications on human evolutionary inference. These algorithms can easily be implemented to discover motifs from multilocus **genotype** data by simple numerical recoding of **genotypes**.

L3 ANSWER 22 OF 57 MEDLINE on STN
Full Text
AN 2005005039 MEDLINE
DN PubMed ID: 15630497
TI The plasminogen activator inhibitor (PAI-1) 4G/5G promoter **polymorphism** and PAI-1 levels in ischemic stroke. A case-control study.
AU van Goor Mary-Lou; Garcia Encarna Gomez; Leebeek Frank; Brouwers Geert-Jan; Koudstaal Peter; Dippel Diederik
CS Erasmus Medical Center Rotterdam, Department of Neurology, PO Box 2040, 3000 CA Rotterdam, The Netherlands.. m.vangoor@erasmusmc.nl
SO Thrombosis and haemostasis, (2005 Jan) Vol. 93, No. 1, pp. 92-6.
Journal code: 7608063. ISSN: 0340-6245.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200507
ED Entered STN: 5 Jan 2005
Last Updated on STN: 6 Jul 2005
Entered Medline: 5 Jul 2005
AB High levels of plasminogen activator inhibitor type 1 (PAI-1) have been implicated as a **risk** factor for **cardiovascular** disease, but its precise role remains controversial. The 4G allele of the PAI-1 4G/5G promoter **polymorphism** is associated with higher levels of PAI-1. We studied the relationship between ischemic stroke and the PAI-1 4G/5G **polymorphism** and PAI-1 antigen levels. We performed a case-control study among patients aged 18-75 years with first ischemic stroke,

confirmed by CT. All patients were screened for **cardiovascular risk** factors, cardiac disorders and large vessel disease. We excluded patients with a definite non-atherosclerotic cause of the stroke and patients using oral anticoagulants. Population-controls were age -and sex-matched, without a history of stroke, and of the Caucasian race. Venous blood samples were taken for PAI-1 4G/5G **polymorphism** and PAI-1 level one week after stroke. We included 124 patients and 125 controls. Mean age was 56 yrs (range 18 to 75 yrs). Sixty one patients (50%) and 58 (47%) controls were heterozygous for the PAI-1 4G/5G **polymorphism**. The homozygous 4G/4G **genotype** was found in 33 patients (27%) and in 36 controls (29%). The odds ratio of ischemic stroke associated with 4G-carriers versus 5G/5G homozygotes was 1.0 (95% CI: 0.6-1.8). The **relative risk** of ischemic stroke associated with the level of PAI-1 in the upper quartile was 0.73 (95%CI: 0.4 to 1.4). Neither the PAI-1 4G/5G **polymorphism** nor the PAI-1 antigen level is a strong **risk** factor for ischemic stroke.

L3 ANSWER 23 OF 57 MEDLINE on STN
Full Text
AN 2004518064 MEDLINE
DN PubMed ID: 15241484
TI Effect of genetic variation in the human S-adenosylhomocysteine hydrolase gene on total homocysteine concentrations and **risk** of recurrent venous thrombosis.
AU Gellekink Henkjan; den Heijer Martin; Kluijtmans Leo A J; Blom Henk J
CS Laboratory of Pediatrics and Neurology, University Medical Center Nijmegen, The Netherlands.
SO European journal of human genetics : EJHG, (2004 Nov) Vol. 12, No. 11, pp. 942-8.
Journal code: 9302235. ISSN: 1018-4813.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200505
ED Entered STN: 19 Oct 2004
Last Updated on STN: 12 May 2005
Entered Medline: 11 May 2005
AB Hyperhomocysteinemia is an independent and graded **risk** factor for arterial vascular disease and venous thrombosis. It is still debated via which mechanism homocysteine (Hcy) causes vascular disease. S-adenosylhomocysteine hydrolase (AHCY) catalyses the reversible hydrolysis of S-adenosylhomocysteine (AdoHcy) to Hcy. As an increase in AdoHcy, a strong inhibitor of many methyltransferases, is observed in hyperhomocysteinemic individuals, AdoHcy may play a role in the development of **cardiovascular** diseases by inhibiting transmethylation reactions. We sequenced the entire coding region and parts of the untranslated regions (UTRs) of the AHCY gene of 20 patients with recurrent venous thrombosis in order to identify genetic variation within this gene. We identified three sequence variants in the AHCY gene: a C > T transition in the 5' UTR (-34 bp C > T), a missense mutation in exon 2, which mandates an amino-acid conversion at codon 38 (112 C > T; Arg38Trp) and a silent mutation in exon 4 (390 C > T; Asp130Asp). We studied the effect of the first two variants on total plasma Hcy and venous thrombosis **risk** in a case-control study on recurrent venous thrombosis. The two **polymorphisms** under study seem to have no evident effect on tHcy. The adjusted **relative risk** of venous thrombosis associated with the 112CT **genotype** compared with 112CC individuals was 1.27 (95% CI 0.55-2.94), whereas the -34CT **genotype** confers a **risk** of 1.25 (95% CI 0.44-3.52) compared with the wild-type **genotype** at this locus. However, the wide confidence intervals do not allow firm conclusions to be drawn.

L3 ANSWER 24 OF 57 MEDLINE on STN
Full Text
AN 2004467243 MEDLINE
DN PubMed ID: 15377476
TI G20210A prothrombin gene variant and clinical outcome in patients with a first acute coronary syndrome.
AU Burzotta Francesco; Leone Antonio Maria; Paciaroni Katia; De Stefano Valerio; Rossi Elena; Testa Luca; Giannico Floriana; Leone Giuseppe; Maseri Attilio; Crea Filippo; Andreotti Felicita
CS Institute of Cardiology, Catholic University, Rome, Italy..

f.burzotta@eudoramail.com
SO Haematologica, (2004 Sep) Vol. 89, No. 9, pp. 1134-8.
Journal code: 0417435. E-ISSN: 1592-8721.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200604
ED Entered STN: 21 Sep 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 26 Apr 2006
AB BACKGROUND AND OBJECTIVES: The prognostic value of the G20210A prothrombin gene **polymorphism** in patients with a first acute coronary syndrome has not been previously assessed. We conducted a prospective study to investigate this issue. DESIGN AND METHODS: **Genotyping** at the 20210 prothrombin gene locus was performed in 162 patients with a first episode of myocardial infarction (MI) or unstable angina (UA) occurring before 65 years of age. Patients were stratified according to **cardiovascular risk** factors and to treatment strategy. The subsequent two-year **relative risk** (RR) of adverse events (death, MI and UA) was adjusted for possible confounders and analyzed according to **genotype**, **risk** factor category, and treatment allocation. RESULTS: In the entire study population, the prothrombin variant did not significantly increase the two-year **risk** of events: the adjusted RR for GA vs GG carriers was 1.82 (95% CI 0.68-4.89). However, in the absence of traditional **cardiovascular risk** factors the **risk** of events was consistently higher: among the 46 patients without hypertension, diabetes and hypercholesterolemia, GA vs GG carriership was associated with an adjusted RR at two years of 5.64 (95% CI 1.07-29.84). The gene variant also enhanced the **risk** of events among the 98 patients who did not undergo myocardial revascularization procedures (RR for GA vs GG: 2.89, 95% CI 1.04-8.00), but not among those who did. INTERPRETATION AND CONCLUSIONS: The present prospective study suggests that heterozygosity for the G20210A prothrombin **polymorphism** adversely affects prognosis after a first acute coronary syndrome in the subgroup of patients without metabolic **risk** factors and in those not treated by revascularization procedures.

L3 ANSWER 25 OF 57 MEDLINE on STN
Full Text
AN 2004461430 MEDLINE
DN PubMed ID: 15282206
TI A common haplotype at the CD36 locus is associated with high free fatty acid levels and increased **cardiovascular risk** in Caucasians.
AU Ma Xiaowei; Bacci Simonetta; Mlynarski Wojciech; Gottardo Lucia; Soccio Teresa; Menzaghi Claudia; Iori Elisabetta; Lager Robert A; Shroff Adhir R; Gervino Ernest V; Nesto Richard W; Johnstone Michael T; Abumrad Nada A; Avogaro Angelo; Trischitta Vincenzo; Doria Alessandro
CS Research Division, Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA.
NC DK36836 (United States NIDDK)
DK60837 (United States NIDDK)
HL71981 (United States NHLBI)
HL73168 (United States NHLBI)
SO Human molecular genetics, (2004 Oct 1) Vol. 13, No. 19, pp. 2197-205.
Electronic Publication: 2004-07-28.
Journal code: 9208958. ISSN: 0964-6906.
CY England: United Kingdom
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200502
ED Entered STN: 17 Sep 2004
Last Updated on STN: 18 Feb 2005
Entered Medline: 17 Feb 2005
AB CD36 is a class B scavenger receptor recognizing a variety of ligands including long-chain fatty acids and modified LDL. We investigated whether genetic variability at this locus is a determinant of free fatty acid (FFA) plasma levels and **risk** of coronary artery disease (CAD) in

Caucasians. Typing of 21 polymorphic markers, evenly spanning the CD36 gene, revealed two linkage disequilibrium (LD) blocks that could be tagged by five **polymorphisms** (-33137A>G, -31118G>A, 25444G>A, 27645del>ins and 30294G>C). In 585 non-diabetic individuals of Caucasian origin, the 30294G>C **polymorphism** was significantly associated with FFA levels (P = 0.02)--an effect that was especially visible among men (P = 0.009). A similar association was observed in this gender at -33137 (P = 0.008) and -31118 (P = 0.028). When the five tag **polymorphisms** were considered together, men carrying the AGGIG haplotype had 31% higher FFA (P = 0.0002) and 20% higher triglycerides (P = 0.025) than non-carriers. The same haplotype was associated with increased **risk** of CAD in 197 type 2 diabetic individuals from the US (OR = 2.3, 95% CI 1.2-4.2). A similar tendency was observed in a group of 321 type 2 diabetic individuals from Italy (OR = 1.4, 0.9-2.3), resulting in an overall **relative risk** of 1.6 (1.1-2.3, P = 0.015) in the two populations considered together. By targeted resequencing, we identified a common variant in the CD36 promoter that is in strong LD with the AGGIG haplotype and could be partly responsible for these findings. In conclusion, this comprehensive study of CD36 variability indicates that the common **polymorphisms** at this locus modulate lipid metabolism and **cardiovascular risk** in Caucasians.

L3 ANSWER 26 OF 57 MEDLINE on STN
Full Text
AN 2004311821 MEDLINE
DN PubMed ID: 15213208
TI Estrogen receptor alpha gene **polymorphisms** and **risk** of myocardial infarction.
AU Schuit Stephanie C E; Oei Hok-Hay S; Witteman Jacqueline C M; Geurts van Kessel Corine H; van Meurs Joyce B J; Nijhuis Rogier L; van Leeuwen Johannes P T M; de Jong Frank H; Zillikens M Carola; Hofman Albert; Pols Huibert A P; Uitterlinden Andre G
CS Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands.
SO JAMA : the journal of the American Medical Association, (2004 Jun 23) Vol. 291, No. 24, pp. 2969-77.
Journal code: 7501160. E-ISSN: 1538-3598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200406
ED Entered STN: 25 Jun 2004
Last Updated on STN: 29 Jun 2004
Entered Medline: 28 Jun 2004
AB CONTEXT: The role of estrogens in ischemic heart disease (IHD) is uncertain. Evidence suggests that genetic variations in the estrogen receptor alpha (ESR1) gene may influence IHD **risk**, but the role of common sequence variations in the ESR1 gene is unclear. OBJECTIVE: To determine whether the ESR1 haplotype created by the c.454-397T>C (PvuII) and c.454-351A>G (XbaI) **polymorphisms** is associated with myocardial infarction (MI) and IHD **risk**. DESIGN, SETTING, AND PARTICIPANTS: In 2617 men and 3791 postmenopausal women from The Rotterdam Study (enrollment between 1989-1993 and follow-up to January 2000), a population-based, prospective cohort study of participants aged 55 years and older, ESR1 c.454-397T>C and c.454-351A>G haplotypes were determined. Detailed interviews and physical examinations were performed, blood samples were obtained, and **cardiovascular risk** factors were assessed. MAIN OUTCOME MEASURE: The primary outcome was MI and IHD defined as MIs, revascularization procedures, and IHD mortality. RESULTS: Approximately 29% of women and 28.2% of men were homozygous carriers of the ESR1 haplotype 1 (-397 T and -351 A) allele, 49% of women and 50% of men were heterozygous carriers, and 22% of women and 21.4% of men were noncarriers. During a mean follow-up of 7.0 years, 285 participants (115 women; 170 men) had MI, and 440 (168 women; 272 men) had an IHD event, of which 97 were fatal. After adjustment for known **cardiovascular risk** factors, female heterozygous carriers of haplotype 1 had an increased **risk** of MI (event rate, 2.8%; **relative risk** [RR], 2.23; 95% confidence interval [CI], 1.13-4.43) compared with noncarriers (event rate, 1.3%), whereas homozygous carriers had an increased **risk** (event rate, 3.2%; RR, 2.48; 95% CI, 1.22-5.03). For IHD events, we observed a similar association. In women, the effect of haplotype 1 on fatal IHD was larger than on

nonfatal IHD. In men, the ESR1 haplotypes were not associated with an increased **risk** of MI (event rate, 5.7%; RR, 0.93; 95% CI, 0.59-1.46 for heterozygous carriers; and event rate, 5.1%; RR, 0.82; 95% CI, 0.49-1.38 for homozygous carriers) compared with noncarriers (event rate, 5.8%) and were not associated with an increased **risk** of IHD. CONCLUSIONS: In this population-based, prospective cohort study, postmenopausal women who carry ESR1 haplotype 1 (c.454-397 T allele and c.454-351 A allele) have an increased **risk** of MI and IHD, independent of known **cardiovascular risk** factors. In men, no association was observed.

L3 ANSWER 27 OF 57 MEDLINE on STN
Full Text
AN 2004307800 MEDLINE
DN PubMed ID: 15211444
TI Association between ENOS gene **polymorphism** and **cardiovascular** events in nondiabetic hemodialysis patients: a prospective study.
AU Asakimori Yukiteru; Yorioka Noriaki; Tanaka Junko; Takasugi Norihisa; Harada Satoru; Shigemoto Kenichiro; Yamashita Kazuomi; Usui Koji; Arita Michiko; Kohno Nobuoki
CS Department of Molecular and Internal Medicine , Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan.
SO American journal of kidney diseases : the official journal of the National Kidney Foundation, (2004 Jul) Vol. 44, No. 1, pp. 112-20.
Journal code: 8110075. E-ISSN: 1523-6838.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200410
ED Entered STN: 24 Jun 2004
Last Updated on STN: 27 Oct 2004
Entered Medline: 26 Oct 2004
AB BACKGROUND: Synthesis of nitric oxide by endothelial nitric oxide synthase (ENOS) plays a key role in the atherosclerotic process. Several **polymorphisms** of the gene encoding ENOS are now known and have been investigated with respect to their influence on **cardiovascular** disease **risk** in the general population. The authors prospectively investigated whether ENOS gene **polymorphisms** determined the **risk** of **cardiovascular** complications in a cohort of hemodialysis patients. METHODS: A total of 335 nondiabetic hemodialysis patients were **genotyped** for 3 ENOS **polymorphisms** (T-786-->C, intron 4, and Glu298Asp **polymorphism**) and were followed up prospectively for a mean of 44.2 +/- 9.0 months. The end-points of the study were major cardiac, cerebrovascular, or peripheral vascular events. RESULTS: Two ENOS **polymorphisms** were associated with **cardiovascular** events: a T to C substitution at position -786 of the promoter and a deletion-insertion in intron 4 (the a allele having 4 repeats of a consensus sequence and the b allele having 5 repeats). A total of 84 subjects were -786C carriers (CC+TC), and 15 (18%) suffered from **cardiovascular** events compared with only 13 of 251 TT patients (5%). The **relative risk** of **cardiovascular** events was higher for -786C carriers compared with noncarriers (**relative risk**: 2.05, P = 0.0003). It was also higher for a allele carriers (intron 4 **polymorphism**) compared with noncarriers (**relative risk**: 1.97, P = 0.0005). CONCLUSION: T-786-->C **polymorphism** and intron 4 **polymorphism**, but not Glu298Asp **polymorphism**, of the ENOS gene can influence the **risk** of **cardiovascular** events in Japanese nondiabetic hemodialysis patients.

L3 ANSWER 28 OF 57 MEDLINE on STN
Full Text
AN 2003578529 MEDLINE
DN PubMed ID: 14660992
TI The cholesteryl ester transfer protein Taq1B gene **polymorphism** predicts clinical benefit of statin therapy in patients with significant coronary artery disease.
AU Carlquist John F; Muhlestein Joseph B; Horne Benjamin D; Hart Noal I; Bair Tami L; Molhuizen Henri O F; Anderson Jeffrey L
CS Cardiovascular Department, LDS Hospital, Salt Lake City, Utah 84143, USA.. ldjcarlq@ihc.com
SO American heart journal, (2003 Dec) Vol. 146, No. 6, pp. 1007-14.
Journal code: 0370465. E-ISSN: 1097-6744.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200401
ED Entered STN: 16 Dec 2003
Last Updated on STN: 14 Jan 2004
Entered Medline: 13 Jan 2004
AB BACKGROUND: Cholesteryl ester transfer protein (CETP) regulates plasma lipid distribution. A **polymorphism** in the CETP gene (Taq1B) is associated with CETP activity, HDL concentration, atherosclerosis progression, and response to statins, and may influence **cardiovascular** (CV) events. We studied CETP Taq1B **genotype**, plasma HDL, and clinical events among all patients and patients stratified by statin treatment. METHODS: Consenting patients (n = 2531) with significant coronary artery disease (> or =1 lesion of > or =70% stenosis) undergoing coronary arteriography were **genotyped**, grouped by statin prescription at hospital discharge, and prospectively followed-up for the outcomes of all-cause mortality and myocardial infarction. RESULTS: CETP Taq1B **genotype** frequencies were: B1B1, 32.9%; B1B2, 50.3%; and B2B2 16.8%. Plasma HDL was reduced for B1B1 patients (33 +/- 12 mg/dL, vs 36 +/- 13 mg/dL and 36 +/- 13 mg/dL for B1B2 and B2B2, respectively, P for trend =.003). Overall, event rates did not differ between **genotypes**. Event rates were similar among untreated (24.8%) and statin-treated (24.2%) B1 homozygotes (P = NS); statins significantly reduced events for B1B2 subjects (28.0% vs 21.0%, P =.009) and for B2B2 subjects (26.4% vs 17.4%, P =.048). Therapeutic benefit for B2 carriers remained after adjustment for covariates, and regression interaction analysis showed that B2 carriers experienced reduced events (**relative risk** [RR] 0.62, 95% CI 0.45-0.86), but statins did not benefit those with B1B1 (RR 1.09, 95% CI 0.70-1.7; P for interaction =.02). Findings were similar for the end point of death alone, although a modest benefit was seen in B1B1 patients (RR 0.67, P =.10), in addition to the strong benefit for B1B2 (RR 0.53, P =.001) and B2B2 (RR 0.28, P =.001). CONCLUSIONS: The CETP Taq1B **polymorphism** is associated with differential HDL levels but no significant differential in CV **risk** in the absence of treatment. Importantly, however, CV event reduction by statin therapy is substantially enhanced in the presence of a B2 allele. Our findings suggest, for the first time, the potential of CETP Taq1B **genotyping** to enable more effective, pharmacogenetically directed therapy.

L3 ANSWER 29 OF 57 MEDLINE on STN
Full Text
AN 2003577694 MEDLINE
DN PubMed ID: 14605330
TI 4G/4G **genotype** of PAI-1 gene is associated with reduced **risk** of stroke in elderly.
AU Hoekstra Tiny; Geleijnse Johanna M; Kluft Cornelis; Giltay Erik J; Kok Frans J; Schouten Evert G
CS Division of Human Nutrition, Wageningen University, Netherlands.
SO Stroke; a journal of cerebral circulation, (2003 Dec) Vol. 34, No. 12, pp. 2822-8. Electronic Publication: 2003-11-06.
Journal code: 0235266. E-ISSN: 1524-4628.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 16 Dec 2003
Last Updated on STN: 6 Jan 2004
Entered Medline: 5 Jan 2004
AB BACKGROUND AND PURPOSE: Plasminogen activator inhibitor type 1 (PAI-1) is the main inhibitor of fibrinolysis, and high levels may increase the **risk** of **cardiovascular** disease. The 4G/5G **polymorphism** affects PAI-1 gene transcription with lower levels of plasma PAI-1 in the presence of the 5G allele. We investigated whether plasma PAI-1 and 4G/5G **genotype** would predict the occurrence of **cardiovascular** events at old age. METHODS: **Relative risks** for **cardiovascular** events and all-cause mortality were obtained in strata of PAI-1 activity and 4G/5G **genotype** in a population-based study of 637 Dutch elderly with 7.8 years of follow-up. RESULTS: The 4G/4G **genotype** was associated with a

decreased **risk** of stroke (**relative risk** [RR]=0.4; 95% CI, 0.2 to 0.9), transient ischemic attack (RR=0.3; 95% CI, 0.1 to 0.8), and **cardiovascular** mortality (RR=0.5; 95% CI, 0.3 to 1.0) after adjustment for age, sex, and time of blood sampling. 4G carriers had an increased **risk** of myocardial infarction, but this was not statistically significant. Subjects with high plasma PAI-1 activity were at increased **risk** of stroke (RR=3.3 in highest versus lowest tertile; 95% CI, 1.5 to 7.1), **cardiovascular** mortality (RR=2.3; 95% CI, 1.2 to 4.4), and all-cause mortality (RR=1.5; 95% CI, 1.1 to 2.1). CONCLUSIONS: Our results provide support for a protective effect of the 4G allele against stroke, which is notable given the direct relationship between stroke and PAI-1 activity. We hypothesize that a local increase in tissue PAI-1 associated with the 4G allele may stabilize plaques, thereby reducing the **risk** of cerebrovascular disease.

L3 ANSWER 30 OF 57 MEDLINE on STN
Full Text
AN 2003454185 MEDLINE
DN PubMed ID: 14514737
TI Role of the endothelin-1 gene locus for renal impairment in the general nondiabetic population.
AU Pinto-Sietsma Sara-Joan; Herrmann Stefan-Martin; Schmidt-Petersen Klaus; Niu Tianhua; Hillege Hans L; Janssen Wilbert M T; de Zeeuw Dick; de Jong Paul; Kreutz Reinhold
CS Department of Internal Medicine, Division of Nephrology, Academic Hospital Groningen, University Groningen, Groningen, The Netherlands.
SO Journal of the American Society of Nephrology : JASN, (2003 Oct) Vol. 14, No. 10, pp. 2596-602.
Journal code: 9013836. ISSN: 1046-6673.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200409
ED Entered STN: 30 Sep 2003
Last Updated on STN: 15 Sep 2004
Entered Medline: 14 Sep 2004
AB A decreased GFR in the range of mild renal insufficiency and an increased urinary albumin excretion (UAE) rate in the range of microalbuminuria are important **cardiovascular risk** factors. Endothelin-1 (ET-1) has been suggested to be a major disease promoting factor in renal disease. The role of the ET-1 gene locus (EDN1) for renal function in the general nondiabetic population was evaluated. To explore the overall relevance of EDN1, two suitable single-nucleotide **polymorphisms**, EDN1 K198N and EDN1 T-1370G, were selected, and haplotype analysis was performed. Determined were **genotypes** in 7291 nondiabetic subjects from the Prevention of Renal and Vascular End-Stage Disease (PREVEND) study. Genetic analysis was related to UAE and GFR as continuous variables and to microalbuminuria and diminished filtration as dichotomous traits. In a logistic regression analysis, no significant higher **risk** for increased UAE, microalbuminuria, decreased GFR, or diminished filtration could be observed for either single-nucleotide **polymorphism** separately. Haplotype analysis revealed that individuals with the homozygous G-N haplotype (compound EDN1 -1370GG/198NN **genotype**) have a lower GFR than the remaining subjects ($P < 0.05$) and exhibit a significant higher **risk** for the presence of a diminished filtration (**relative risk**, 2.4; 95% confidence interval, 1.07 to 5.33; $P < 0.05$). Further analysis demonstrated no association between this haplotype and UAE or plasma ET-1 levels. Although a functional relevance of the EDN1 G-N haplotype itself remains unclear, the data demonstrate that genetic variation at the EDN1 locus has a significant effect on glomerular filtration but not on UAE in the general nondiabetic population.

L3 ANSWER 31 OF 57 MEDLINE on STN
Full Text
AN 2003399687 MEDLINE
DN PubMed ID: 12932598
TI Platelet glycoprotein IIb/IIIa Pl(A2)/Pl(A2) homozygosity associated with **risk** of ischemic **cardiovascular** disease and myocardial infarction in young men: the Copenhagen City Heart Study.
AU Bojesen Stig E; Juul Klaus; Schnohr Peter; Tybjaerg-Hansen Anne;

Nordestgaard Borge G
CS Department of Clinical Biochemistry, Herlev University Hospital, Herlev, Denmark. (Copenhagen City Heart Study).
SO Journal of the American College of Cardiology, (2003 Aug 20) Vol. 42, No. 4, pp. 661-7.
Journal code: 8301365. ISSN: 0735-1097.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200309
ED Entered STN: 27 Aug 2003
Last Updated on STN: 1 Oct 2003
Entered Medline: 30 Sep 2003
AB OBJECTIVES: We tested the hypothesis that platelet glycoprotein (GP) IIb/IIIa Pl(A2)/Pl(A2) homozygotes or Pl(A1)/Pl(A2) heterozygotes versus Pl(A1)/Pl(A1) noncarriers have increased **risk** of ischemic **cardiovascular** disease and myocardial infarction (MI), stratified for age and gender. BACKGROUND: The GP IIb/IIIa Pl(A1)/Pl(A2) **polymorphism** influences aggregation of platelets; however, an association between ischemic **cardiovascular** disease and heterozygosity remains controversial, and association with homozygosity is largely unexplored. METHODS: We **genotyped** the participants of the Copenhagen City Heart Study, a prospective **cardiovascular** investigation of the Danish general population (n = 9,149, 22-year follow-up) and assessed the **risk** of ischemic **cardiovascular** disease in heterozygotes or homozygotes versus noncarriers. RESULTS: Of the participants, 70.0%, 27.3%, and 2.7% were noncarriers, heterozygotes, or homozygotes, respectively. Incidence of ischemic **cardiovascular** disease was 167 and 103 per 10,000 person-years in homozygous and noncarrier men (log-rank: p = 0.006), whereas this difference was not observed in women (p = 0.33) (**genotype**.gender interaction: p = 0.03). In homozygous versus noncarrier men <40 years of age, 40 to 50 years, and >50 years at entry, age-adjusted **relative risks** (RRs) of ischemic **cardiovascular** disease were 3.6 (1.4 to 9.0), 2.4 (1.3 to 4.6), and 1.0 (0.6 to 1.8), respectively (age.**genotype** interaction in men: p = 0.04); equivalent multifactorially adjusted RRs were 3.0 (1.1 to 8.0), 2.0 (1.0 to 3.9), and 1.0 (0.6 to 1.8), respectively. The corresponding age-adjusted RR values of MI in men were 5.2 (1.5 to 18), 3.5 (1.6 to 7.5), and 0.5 (0.1 to 1.5), respectively (age.**genotype** interaction in men: p = 0.002); equivalent multifactorially adjusted RRs were 3.8 (1.0 to 15), 3.1 (1.4 to 6.9), and 0.5 (0.2 to 1.5), respectively. CONCLUSIONS: Pl(A2)/Pl(A2) homozygosity is associated with a three-fold and four-fold **risk** of ischemic **cardiovascular** disease and MI in young men.

L3 ANSWER 32 OF 57 MEDLINE on STN
Full Text
AN 2003288410 MEDLINE
DN PubMed ID: 12767551
TI Association of two angiotensinogen gene **polymorphisms**, M235T and G(-6)A, with chronic heart failure.
AU Goldbergova Monika; Spinarova Lenka; Spinar Jindrich; Toman Jiri; Vasku Anna; Vacha Jiri
CS lnstitute of Pathological Physiology, Faculty of Medicine, Masaryk University Brno, Komenskeho nam.2, 662 43, Brno, Czech Republic. goldberg@med.muni.cz. <goldberg@med.muni.cz>
SO International journal of cardiology, (2003 Jun) Vol. 89, No. 2-3, pp. 267-72.
Journal code: 8200291. ISSN: 0167-5273.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 21 Jun 2003
Last Updated on STN: 31 Oct 2003
Entered Medline: 30 Oct 2003
AB The aim of the study was to focus on the relationship between the angiotensinogen (AGT) gene **polymorphisms**, M235T and promoter G(-6)A, and chronic heart failure in the Czech population. A total of 158 patients

with chronic heart failure (functional class NYHA II-IV, ejection fraction <40%, cardiothoracic index >50%) were compared with a control group of 200 subjects of similar age and sex distribution, without any personal history of **cardiovascular** diseases. The AGT gene **polymorphisms** were detected by polymerase chain reaction (PCR) and restriction fragment length **polymorphism** (RFLP) methods. No significant differences in distributions of AGT **genotypes** between patients with chronic heart failure (CHF) and controls were found. The differences in distributions of alleles in AGT M235T (P(a)=0.02) and **genotypes** in AGT G(-6)A (P(g)=0.017) were found within women groups. Within CHF patients the distribution of AGT G(-6)A **genotypes** was not consistent with Hardy-Weinberg equilibrium (P=0.0001). We found significant **relative risk** of CHF in the GGMT **genotype**, OR=2.63 with 95% CI 1.39-4.95, P(corr)=0.01 (in the male group OR=1.83, 95% CI 0.92-3.66, P(corr)=0.3; in the female group OR=15.5, 95% CI 1.86-129.42, P(corr)=0.008). We provide evidence of increased **risk** in subjects with the GGMT variant of associated **genotype** of AGT gene for CHF, especially of fifteen-fold **risk** of this variant in women.

L3 ANSWER 33 OF 57 MEDLINE on STN
Full Text
AN 2003266097 MEDLINE
DN PubMed ID: 12790760
TI Office blood pressure, heart rate and A(-596)G interleukin-6 gene **polymorphism** in apparently healthy Czech middle-aged population.
AU Vasku A; Soucek M; Goldbergova M; Vacha J
CS Institute of Pathological Physiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic.. avasku@med.muni.cz
SO Physiological research / Academia Scientiarum Bohemoslovaca, (2003) Vol. 52, No. 3, pp. 291-7.
Journal code: 9112413. ISSN: 0862-8408.
CY Czech Republic
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 8 Jun 2003
Last Updated on STN: 23 Apr 2004
Entered Medline: 22 Apr 2004
AB The aim of the study was to assess the association between promoter **polymorphism** [A(-596)G] in interleukin-6 gene and office systolic and diastolic blood pressures, and the heart rate (HR) in apparently healthy Czech subjects. Furthermore, we evaluated the possible influence of gender, BMI and smoking on these supposed associations. An age-matched (40-50 years) and gender-matched (F/M=81/89) sample of apparently healthy Czech subjects (n=170, F/M=81/89) without hypertension, other **cardiovascular** diseases or diabetes was examined. The A(-596)G Il-6 gene **polymorphism** was detected by the PCR method. No differences in **genotype** distribution and/or allelic frequency was found between groups with lower systolic blood pressure (L 122 mm Hg) and higher systolic blood pressure (> 122 mm Hg). Similarly, no differences in the IL-6 **polymorphism** were found between lower (L 86 mm Hg) and higher (> 86 mm Hg) diastolic blood pressure groups. However, we proved a significant increase of **genotypes** AG+GG as well as the allele (-596)G in higher (>78 beats/min) heart rate group. The **genotypes** AG+GG represent significantly higher **relative risk** for higher HR frequency, especially in women. Among lean persons with a low heart rate frequency, fewer AG+GG **genotypes** were determined than among any other subjects. The **genotypes** AG+GG are more frequent in non-smoking persons with higher HR compared to non-smoking subjects with lower HR, especially in women. Gender, BMI and smoking substantially modify the distribution of A(-596)G Il-6 gene **polymorphism** in apparently healthy persons with lower or higher heart rate.

L3 ANSWER 34 OF 57 MEDLINE on STN
Full Text
AN 2003111571 MEDLINE
DN PubMed ID: 12624641
TI Association between TAFI antigen and Ala147Thr **polymorphism** of the TAFI gene and the angina pectoris incidence. The PRIME Study (Prospective Epidemiological Study of MI).

AU Morange Pierre E; Juhan-Vague Irene; Scarabin Pierre Y; Alessi Marie C; Luc Gerald; Arveiler Dominique; Ferrieres Jean; Amouyel Philippe; Evans Alun; Ducimetiere Pierre
CS Department of Hematology, Hospital de la Timone, INSERM 99-36 Marseilles, France. (PRIME Study group).
SO Thrombosis and haemostasis, (2003 Mar) Vol. 89, No. 3, pp. 554-60. Journal code: 7608063. ISSN: 0340-6245.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 8 Mar 2003
Last Updated on STN: 31 Oct 2003
Entered Medline: 30 Oct 2003
AB Thrombin activatable fibrinolysis inhibitor (TAFI), a recently described inhibitor of fibrinolysis, has been hypothesized as playing a role in atherothrombosis. However, the evidence from retrospective studies, which have evaluated the role of TAFI in vascular **risk**, is conflicting. In a prospective cohort (the PRIME Study) of nearly 10 000 apparently healthy men recruited in France (Lille, Strasbourg, Toulouse) and Northern Ireland (Belfast), we measured baseline plasma concentration of TAFI antigen among 143 participants (81 from France and 62 from Ireland) who subsequently developed angina pectoris and among 286 age-matched participants who remained free of disease during the 5 years of follow-up. **Genotyping** of the Ala147Thr **polymorphism** located in the TAFI gene was performed using an allele specific PCR. In France, mean levels of TAFI were significantly higher at baseline among men who subsequently developed angina pectoris compared with their control subjects (119 versus 107 %; p = 0.02). The **risk** of future angina pectoris increased with increasing tertiles of TAFI (p = 0.02), such that men in the highest tertile at study entry had a 5-fold higher **relative risk** than those in the lowest tertile (95% confidence interval, 1.38 to 18.58) after controlling for the conventional **cardiovascular risk** factors. No such difference was observed in Northern Ireland. In France, Thr/Thr carriers of the Ala147Thr **polymorphism** were significantly more frequent in cases than in controls (p = 0.01) leading to a **relative risk** of angina pectoris of 2.7 (95%CI 1.2-5.8). Increase in plasma TAFI antigen levels is a **risk** factor for angina pectoris in France. **Genotyping** for the Ala147Thr **polymorphism** seems to be a reliable tool to assess the **risk** mediated by TAFI.

L3 ANSWER 35 OF 57 MEDLINE on STN
Full Text
AN 2003069637 MEDLINE
DN PubMed ID: 12566975
TI Association between the G protein beta3 subunit 825t allele and radial artery hypertrophy.
AU Hanon Olivier; Luong Vu; Mourad Jean Jacques; Bortolotto Luiz A; Safar Michel; Girerd Xavier
CS Department of Internal Medicine and INSERM U337, Broussais Hospital, 96 rue Didot, F-75014 Paris, France.
SO Journal of vascular research, (2002 Nov-Dec) Vol. 39, No. 6, pp. 497-503. Journal code: 9206092. ISSN: 1018-1172.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 14 Feb 2003
Last Updated on STN: 7 Mar 2003
Entered Medline: 6 Mar 2003
AB The GNB3 C825T gene **polymorphism** has recently been identified and associated with hypertension, obesity and left ventricular hypertrophy. The aim of the study was to determine the relationship between the C825T **polymorphism** of the gene encoding for the G protein beta3 subunit (GNB3 C825T) and vascular hypertrophy. We studied a cohort of 306 subjects (age 49 +/- 12 years) without evidence of **cardiovascular** disease and never treated with **cardiovascular** drugs. Vascular phenotypes were evaluated for the common carotid and radial arteries using high-resolution echo-tracking devices. **Genotype** frequencies were in agreement with the

Hardy-Weinberg equilibrium. For the radial artery, mean wall thickness was significantly higher in subjects carrying the 825T allele than in CC **genotype** subjects (240 +/- 54 microm for CT **genotype** and 241 +/- 53 microm for TT **genotype** vs. 222 +/- 52 microm for CC **genotype**, p = 0.01). The frequency of the 825T allele was significantly different in subjects with (52%) and without (35%) radial artery hypertrophy (chi(2) = 10.88, p < 0.001). The **relative risk** of radial artery hypertrophy in subjects carrying the 825T allele compared with those with the CC **genotype** was 3.02 (95% CI 1.53- 5.95). A logistic regression analysis indicated that the positive and significant association between the 825T allele and radial artery hypertrophy was independent of age, blood pressure, gender and BMI. In contrast, no association between **genotypes** and carotid artery wall thickening was observed. These results suggest that some genetic characteristics determine in part the patterns of radial artery geometrical changes. As the 825T allele is associated with vascular hypertrophy of a muscular artery but not with structural changes of an elastic artery, we hypothesize that the 825T allele may be a genetic marker of arteriolosclerosis.

L3 ANSWER 36 OF 57 MEDLINE on STN
Full Text
AN 2002664889 MEDLINE
DN PubMed ID: 12425488
TI Angiotensin-converting enzyme (ACE) insertion/deletion **polymorphism** and survival in a cohort of chronic hemodialysis patients.
AU Higashiuesato Y; Tana T; Tozawa M; Iseki C; Iseki K; Fukiyama K; Takishita S
CS Third Department of Internal Medicine, University of the Ryukyus, Okinawa, Japan.. yhigashi-ryk@umin.ac.jp
SO Clinical nephrology, (2002 Nov) Vol. 58, No. 5, pp. 370-5.
Journal code: 0364441. ISSN: 0301-0430.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 12 Nov 2002
Last Updated on STN: 26 Feb 2003
Entered Medline: 25 Feb 2003
AB BACKGROUND: There are conflicting reports regarding the relationship between the angiotensin-converting enzyme (ACE) insertion/deletion (I/D) **polymorphism** and the initiation and progression of **cardiovascular** disease. Moreover, there is no report regarding the relationship between the ACE I/D **polymorphism** and the prognosis of chronic dialysis patients. METHODS: We examined the frequency of the ACE I/D **polymorphism** in 727 chronic hemodialysis patients in Okinawa, Japan, and observed the prognosis over 2 years in 407 men and 320 women with mean age (SD) of 55.5 (13.9) years with a mean duration of dialysis of 84.3 (66.6) months. RESULTS: **Genotype** frequencies were 42.1% for II, 43.2% for ID, and 14.7% for DD. The **relative risks** of death were examined by Cox-proportional hazards analysis after adjusting for age, sex, age at the start of dialysis, presence of diabetes mellitus and hypertension and total cholesterol and serum albumin levels. The adjusted hazard ratio (95% confidence interval) was 1.03 (0.38 - 2.85) for DD **genotype** and 1.50 (0.83 - 2.70) for DD+ID **genotype** when compared to II **genotype**. CONCLUSION: ACE I/D **polymorphism** appears to have no relation to the short-term prognosis in chronic hemodialysis patients.

L3 ANSWER 37 OF 57 MEDLINE on STN
Full Text
AN 2002411177 MEDLINE
DN PubMed ID: 12164877
TI Anti-inflammatory interleukin-10 **genotype** protects dialysis patients from **cardiovascular** events.
AU Girndt Matthias; Kaul Harald; Sester Urban; Ulrich Christof; Sester Martina; Georg Thomas; Kohler Hans
CS Medical Department IV, University of Homburg/Saar, Kirrberger Strasse 1, D-66421 Homburg/Saar, Germany.
SO Kidney international, (2002 Sep) Vol. 62, No. 3, pp. 949-55.
Journal code: 0323470. ISSN: 0085-2538.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(CLINICAL TRIAL)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 8 Aug 2002
Last Updated on STN: 12 Feb 2003
Entered Medline: 11 Feb 2003
AB BACKGROUND: Inflammatory processes play an important role for the progression of atherosclerosis. This can be studied particularly well in patients with chronic renal failure who are on hemodialysis, as they show systemic inflammation due to uremia and dialysis while suffering from premature mortality secondary to rapidly progressing atherosclerosis. Interleukin (IL)-10 is a regulatory cytokine that limits inflammatory processes. The quantitative production of IL-10 is subject to genetic variation based on **polymorphisms** in the promoter of its gene. We tested the hypothesis that the IL-10 **genotype**, by influencing the capacity to compensate for dialysis-induced systemic inflammation, determines the **risk** for **cardiovascular** complications. METHODS: Three hundred chronic hemodialysis patients were **genotyped** for the polymorphic bases at positions -1082 and -819 of the IL-10 promoter sequence. They were prospectively followed for a mean of 20.2 +/- 7.3 months. End-points of the study were major events related to cardiac, cerebrovascular or peripheral artery disease. RESULTS: The -1082A* allele, which is associated with low production of the cytokine IL-10 and elevated markers of systemic inflammation such as C reactive protein, was predictive for a higher **cardiovascular** morbidity (**relative risk** for **cardiovascular** events 2.76, 95% confidence interval 1.31 to 4.17, P = 0.004) compared to the -1082G* **genotype**. CONCLUSION: The IL-10 **genotype** influences the **risk** for **cardiovascular** events in hemodialysis patients and allows the definition of a high **risk** group. The data provide further evidence for a causal role of systemic inflammation for progressive atherosclerosis in dialysis patients.

L3 ANSWER 38 OF 57 MEDLINE on STN
Full Text
AN 2002400011 MEDLINE
DN PubMed ID: 12149201
TI Genetic variability in the extracellular matrix as a determinant of **cardiovascular risk**: association of type III collagen COL3A1 **polymorphisms** with coronary artery disease.
AU Muckian Clare; Fitzgerald Anthony; O'Neill Anne; O'Byrne Anna; Fitzgerald Desmond J; Shields Denis C
CS Department of Clinical Pharmacology, Royal College of Surgeons in Ireland, Dublin.
SO Blood, (2002 Aug 15) Vol. 100, No. 4, pp. 1220-3.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200209
ED Entered STN: 1 Aug 2002
Last Updated on STN: 13 Sep 2002
Entered Medline: 12 Sep 2002
AB Although common genetic variants in platelet collagen receptors influence platelet activation and thrombosis, the impact of **polymorphisms** in collagen genes on **cardiovascular** disease is unknown. To evaluate this, we **genotyped** a highly polymorphic intronic tandem repeat of the COL3A1 gene, encoding collagen type III, alpha 1. This revealed 4 common alleles (COL3A1-1, -2, -3, and -4). The 2 populations studied were as follows: (1) a cross-sectional study of 703 acute coronary syndrome (ACS) patients with myocardial infarction (MI) and unstable angina, and (2) a prospective study of 924 Caucasian patients from the OPUS (Orbofiban in Patients with Unstable coronary Syndromes)-TIMI-16 trial of the oral GPIIb/IIIa antagonist orbofiban. In addition, we studied 306 control subjects and 224 patients with stable angina. In the case-control population, COL3A1-4

carriers were protected against ACS (odds ratio [OR] = 0.57, 95% CI = 0.35-0.91, P =.02) and stable angina (OR = 0.35, 95% CI = 0.16-0.74, P =.006). In the OPUS population, allele 4 again appeared protective against composite end points (death, MI, stroke, recurrent ischemia, and urgent rehospitalization) (**relative risk** [RR] = 0.41, 95% CI = 0.17-1.00). There were significant interactions between COL3A1-1 and -3 variants and treatment. Allele COL3A1-3 was associated with an increased **risk** of the composite end point (RR = 1.65, 95% CI = 1.07-2.55) in patients randomized to orbofiban, but appeared protective in placebo patients (RR = 0.53, 95% CI = 0.28-0.98). We conclude that variants in the COL3A1 gene, the product of which is a vessel-wall protein and platelet ligand, modulate the **risk** of coronary artery disease and could also modulate the response to antithrombotic therapy. This is the first reported association between **polymorphisms** of extracellular matrix components and **cardiovascular risk**.

L3 ANSWER 39 OF 57 MEDLINE on STN
Full Text
AN 2002156981 MEDLINE
DN PubMed ID: 11888533
TI A prospective study of TaqIB **polymorphism** in the gene coding for cholesteryl ester transfer protein and **risk** of myocardial infarction in middle-aged men.
AU Liu Simin; Schmitz Christian; Stampfer Meir J; Sacks Frank; Hennekens Charles H; Lindpaintner Klaus; Ridker Paul M; Liu Simm
CS Division of Preventive Medicine, Department of Medicine, Center for Cardiovascular Disease Prevention, Brigham and Women's Hospital and Harvard Medical School, 900 Commonwealth Avenue East, Boston, MA 02215, USA.
NC CA34944 (United States NCI)
CA40360 (United States NCI)
HL-26490 (United States NHLBI)
HL34595 (United States NHLBI)
SO Atherosclerosis, (2002 Apr) Vol. 161, No. 2, pp. 469-74.
Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200205
ED Entered STN: 13 Mar 2002
Last Updated on STN: 25 Feb 2003
Entered Medline: 14 May 2002
AB BACKGROUND: Molecular variations in the gene coding for the cholesteryl ester transfer protein (CETP) such as the TaqIB **polymorphism** are associated with higher plasma high-density lipoprotein (HDL) concentration. However, whether this **polymorphism** is associated with **risk** of myocardial infarction (MI) is uncertain. METHODS AND RESULTS: In a prospective cohort of 14916 apparently healthy men enrolled in the Physicians' Health Study, allelic status for the TaqIB **polymorphism** in the CETP gene was determined among 384 participants who subsequently developed a first MI (cases) and among an equal number of age and smoking-matched participants who remained free of **cardiovascular** disease during follow-up (controls). Overall, the B2B2 **genotype** was present in 17% of the study participants and was associated with higher HDL cholesterol levels (mean mg/dl [+/- S.D.], 45 +/- 11 for the B1B1 **genotype**, 48 +/- 13 for the B1B2 **genotype** and 50 +/- 12 for the B2B2 **genotype**; P=0.01). However, the **risk** of developing MI did not differ significantly across these three **genotypes**. After adjustment for coronary **risk** factors (but not HDL), the **relative risks** for future MI were 1.12(95% CI 0.74-1.70) for the B1B2 **genotype** and 0.95(95% CI 0.54-1.66) for the B2B2 **genotype**, compared with the B1B1 **genotype**. In subgroup analysis of individuals with low HDL levels, B2B2 **genotype** appeared to have a lower **risk** of MI compared with the B1B1 **genotype**. However, participants with high HDL were at lower **risk** of developing MI regardless of their CETP **genotype**. CONCLUSIONS: In this prospective study of apparently healthy middle-aged US men, carriers of the B2 allele of the TaqIB in the CETP gene had higher HDL concentrations, but did not have lower **risk** of MI. CONDENSED ABSTRACT: In a cohort of apparently healthy middle-aged US men, the relation between CETP **genotype** and MI **risk** was prospectively examined in a nested case-control study. After

adjusting for coronary **risk** factors (but not HDL), the 9-year **risk** of developing MI did not differ significantly by **genotype**. Comparing to the B1B1 **genotype**, the **relative risks** for future MI were 1.12 (95% CI 0.74-1.70) for the B1B2 **genotype** and 0.95 (95% CI 0.54-1.66) for the B2B2 **genotype**.

L3 ANSWER 40 OF 57 MEDLINE on STN
Full Text
AN 2002044894 MEDLINE
DN PubMed ID: 11755935
TI The T allele of the missense Glu(298)Asp endothelial nitric oxide synthase gene **polymorphism** is associated with coronary heart disease in younger individuals with high atherosclerotic **risk** profile.
AU Gardemann Andreas; Lohre Jana; Cayci Sevim; Katz Norbert; Tillmanns Harald; Haberbosch Werner
CS Institut fur Klinische Chemie und Pathobiochemie, Klinikum der Justus-Liebig-Universitat Giessen, Gaffky-Strasse 11, 35392 Giessen, Germany.. andreas.gardemann@klinchemie.med.uni-de
SO Atherosclerosis, (2002 Jan) Vol. 160, No. 1, pp. 167-75.
Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 24 Jan 2002
Last Updated on STN: 6 Apr 2002
Entered Medline: 5 Apr 2002
AB AIMS: Nitric oxide (NO) plays a protective role during atherogenesis. In the endothelium, NO is synthesised by the constitutive NO synthase (ecNOS). We analysed the relation of the ecNOS Glu(298)Asp and 4a/b gene **polymorphisms** to coronary artery disease (CAD) and myocardial infarction (MI) in a population of 3250 German subjects (533 healthy controls and 2717 individuals who underwent coronary angiography). RESULTS: Although in the total sample, the ecNOS T allele was not associated with the **risk** of CAD (P=0.054) and the extent of this disease (P=0.078), a restriction to younger individuals (age</=61, mean age) revealed an association of the ecNOS T allele with an increased **risk** of CAD (1.43, 1.05-1.96; P=0.025) and with the severity of this disease (P=0.037). Similar observations were made in various high-**risk** populations. These associations were even more pronounced when the high-**risk** subgroups were restricted to younger individuals. For example, an odds ratio of 7.66 for CAD (95% CI, 2.0-29; P=0.003) was detected in diabetic individuals who were younger than 61 years. Also with respect to MI, the most pronounced associations of the ecNOS T allele with the **risk** of this disease were detected in younger individuals with at least one other **cardiovascular risk** factor. For example, in diabetics younger than 61 years, the **relative risk** for ecNOS T allele carriers was 9.73 (95% CI, 1.8-53; P=0.008). In contrast, the allele frequencies of the ecNOS 4a/b gene variation were essentially the same in controls and in CAD and MI patients. CONCLUSION: The present data extends earlier observations by the findings that predominantly younger T allele carriers of the ecNOS Glu(298)Asp gene **polymorphism** with various coronary high-**risk** profiles had an increased **risk** to suffer CAD and/or MI. In contrast, no evidence was found for an association of the ecNOS 4a/b gene **polymorphism** with coronary heart disease.

L3 ANSWER 41 OF 57 MEDLINE on STN
Full Text
AN 2001682511 MEDLINE
DN PubMed ID: 11728146
TI Mutation in the promoter region of the beta-fibrinogen gene and the **risk** of future myocardial infarction, stroke and venous thrombosis.
AU Blake G J; Schmitz C; Lindpaintner K; Ridker P M
CS The Center for Cardiovascular Disease Prevention, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02215, USA.
NC HL58755 (United States NHLBI)
SO European heart journal, (2001 Dec) Vol. 22, No. 24, pp. 2262-6.
Journal code: 8006263. ISSN: 0195-668X.
CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 3 Dec 2001
Last Updated on STN: 15 Feb 2002
Entered Medline: 14 Feb 2002
AB AIM: **Polymorphisms** in the promoter region of the beta-fibrinogen gene are associated with increased plasma fibrinogen levels. We investigated whether the distribution of the C148T **polymorphism** is associated with an increase in **cardiovascular risk**. METHODS AND RESULTS: In a nested case-control design, the distribution of the C148T **polymorphism** was investigated among 751 participants in the Physicians' Health Study who subsequently developed myocardial infarction, stroke or venous thromboembolism (cases) and among 751 age- and smoking-matched controls over follow-up of 8.6 years. Frequency of the T allele was similar among men who had myocardial infarction (22.7%, P=0.5), stroke (18.4%, P=0.2) or venous thromboembolism (17.0%, P=0.1) compared with those with no **cardiovascular** events (21.5%). The **relative risk** for any vascular event among men homozygous or heterozygous for the T allele compared with men homozygous for the C allele was 0.94 (95% CI 0.76-1.16). We found no evidence of an association between the T allele and myocardial infarction (**relative risk** 1.06; 95% CI 0.82-1.36), stroke (0.87, 0.63-1.21) or venous thromboembolism (0.75; 0.51-1.08). Analysis adjusted for aspirin use and traditional **cardiovascular risk** factors had no significant effect on these findings. CONCLUSION: In a large prospective cohort, carriage of the T allele for the C148T mutation in the beta-fibrinogen promoter gene was not associated with an increased subsequent **risk** of **cardiovascular** events.

L3 ANSWER 42 OF 57 MEDLINE on STN
Full Text
AN 2001555309 MEDLINE
DN PubMed ID: 11602206
TI Variations of **cardiovascular** disease associated genes exhibit sex-dependent influence on human longevity.
AU Tan Q; Yashin A I; Bladbjerg E M; de Maat M P; Andersen-Ranberg K; Jeune B; Christensen K; Vaupel J W
CS Max-Planck Institute for Demographic Research, Rostock, Germany.
SO Experimental gerontology, (2001 Aug) Vol. 36, No. 8, pp. 1303-15.
Journal code: 0047061. ISSN: 0531-5565.
CY England: United Kingdom
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 17 Oct 2001
Last Updated on STN: 22 Jan 2002
Entered Medline: 7 Dec 2001
AB This article investigates the relationship between the polymorphic variations in genes associated with **cardiovascular** disease and longevity in the Danish population. A new procedure that combines both demographic and the individual genetic information in determining the **relative risks** of the observed genetic variations is applied. The sex-dependent influences can be found by introducing sex-specific population survival and incorporating the **risk** of gene-sex interaction. Three genetic **polymorphisms**, angiotensinogen M/T235, blood coagulation factor VII (FVII) R/Q353 and FVII-323ins10, manifest significant influences on survival in males, with reduced hazards of death for carriers of the angiotensinogen M235 allele, the F VII Q353 allele, and the FVII-323P10 allele. The results show that some of these **genotypes** associated with lower **risk** of **CVD** could also reduce the carrier's death rate and contribute to longevity. However, the presence of sex-dependent effects and the fact that major **CVD**-associated genes failed to impose detrimental influence on longevity lead us to concur that the aging process is highly complicated.

L3 ANSWER 43 OF 57 MEDLINE on STN

Full Text
AN 2001435118 MEDLINE
DN PubMed ID: 11303694
TI Methylenetetrahydrofolate reductase gene **polymorphism** and **risk** of premature myocardial infarction.
AU Gulec S; Aras O; Akar E; Tutar E; Omurlu K; Avci F; Dincer I; Akar N; Oral D
CS Medical School of Ankara University, Turkey.
SO Clinical cardiology, (2001 Apr) Vol. 24, No. 4, pp. 281-4.
Journal code: 7903272. ISSN: 0160-9289.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200108
ED Entered STN: 6 Aug 2001
Last Updated on STN: 6 Aug 2001
Entered Medline: 2 Aug 2001
AB BACKGROUND: Elevated plasma homocysteine level is an independent **risk** factor for **cardiovascular** disease. A common mutation (nucleotid 677C-T) in the gene coding for methylenetetrahydrofolate reductase (MTHFR) has been reported to reduce the enzymatic activity of MTHFR and is associated with elevated plasma levels of homocysteine, especially in subjects with low folate intake. HYPOTHESIS: Methylenetetrahydrofolate reductase T/T **genotype** may be a **risk** factor for premature MI in Turkish population who are known to have low folate levels. METHODS: The study group was comprised of 96 men (aged <45 years) with premature myocardial infarction (MI) and 100 age- and gender-matched controls who had no history or clinical evidence of coronary artery disease (CAD) and/or MI. DNA was extracted from peripheral blood and **genotypes** were determined by polymerase chain reaction, restriction mapping with HinfI, and gel electrophoresis. Conventional **risk** factors for CAD were prospectively documented. RESULTS: Allele and **genotype** frequencies among cases and control subjects were compatible with Hardy-Weinberg equilibrium. The frequencies of T/T, C/T, and C/C **genotypes** among patients with MI and control subjects were 15.6, 40.6, and 43.8%, and 5, 35, and 60%, respectively. Multivariate analyses identified smoking, MTHFR C/T **polymorphism**, diabetes mellitus, family history of CAD, and hypertension as the independent predictors of premature MI. Defining patients with non-T/T **genotype** (C/C and C/T combined) as reference, the **relative risk** of MI for subjects with T/T **genotype** was 5.94 (95% confidence interval: 1.96-18.02, p = 0.0016). CONCLUSIONS: Our findings suggest that C677T transition in the MTHFR gene may be a **risk** factor for premature MI in Turkish men.

L3 ANSWER 44 OF 57 MEDLINE on STN
Full Text
AN 2001196287 MEDLINE
DN PubMed ID: 11246885
TI A **polymorphism** in the gene for IGF-I: functional properties and **risk** for type 2 diabetes and myocardial infarction.
AU Vaessen N; Heutink P; Janssen J A; Witteman J C; Testers L; Hofman A; Lamberts S W; Oostra B A; Pols H A; van Duijn C M
CS Department of Epidemiology and Biostatistics, the Center for Biomedical Genetics, Rotterdam, The Netherlands.
SO Diabetes, (2001 Mar) Vol. 50, No. 3, pp. 637-42.
Journal code: 0372763. ISSN: 0012-1797.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200104
ED Entered STN: 10 Apr 2001
Last Updated on STN: 10 Apr 2001
Entered Medline: 5 Apr 2001
AB Evidence is accumulating that low levels of IGF-I play a role in the pathogenesis of type 2 diabetes and **cardiovascular** diseases. We examined the role of a genetic **polymorphism** in the promoter region of the IGF-I gene in relation to circulating IGF-I levels and growth measured as body height, and we studied the relationship of this **polymorphism** with type 2 diabetes and myocardial infarction. The relation between the

IGF-I **polymorphism** and body height was assessed in a population-based sample of 900 subjects from the Rotterdam Study. Within each **genotype** stratum, 50 subjects were randomly selected for a study of the relation of this **polymorphism** with serum IGF-I levels. To assess the **risk** for type 2 diabetes, we studied 220 patients and 596 normoglycemic control subjects. For myocardial infarction, 477 patients with evidence of myocardial infarction on electrocardiogram and 808 control subjects were studied. A 192-bp allele was present in 88% of the population, suggesting that this is the wild-type allele from which all other alleles originated. Body height was, on average, 2.7 cm lower (95% CI for difference -4.6 to -0.8 cm, P = 0.004), and serum IGF-I concentrations were 18% lower (95% CI for difference -6.0 to -1.3 mmol/l, P = 0.003) in subjects who did not carry the 192-bp allele. In noncarriers of the 192-bp allele, an increased **relative risk** for type 2 diabetes (1.7 [95% CI 1.1-2.7]) and for myocardial infarction (1.7 [95% CI 1.1-2.5]) was found. In patients with type 2 diabetes, the **relative risk** for myocardial infarction in subjects without the 192-bp allele was 3.4 (95% CI 1.1-11.3). Our study suggests that a genetically determined exposure to relatively low IGF-I levels is associated with an increased **risk** for type 2 diabetes and myocardial infarction.

L3 ANSWER 45 OF 57 MEDLINE on STN
Full Text
AN 2001047748 MEDLINE
DN PubMed ID: 10998471
TI The paraoxonase Leu-Met54 and Gln-Arg191 gene **polymorphisms** are not associated with the **risk** of coronary heart disease.
AU Gardemann A; Philipp M; Hess K; Katz N; Tillmanns H; Haberbosch W
CS Institut fur Klinische Chemie und Pathobiochemie, Klinikum der Justus-Liebig-Universitat Giessen, Gaffky-Strasse 11, 35392, Giessen, Germany.
SO Atherosclerosis, (2000 Oct) Vol. 152, No. 2, pp. 421-31.
Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200012
ED Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 7 Dec 2000
AB BACKGROUND: Evidence has been presented that gene **polymorphisms** (PON54 L/M, PON191 Q/R) of paraoxonase are **risk** factors of coronary heart disease. RESULTS: We determined both PON **genotypes** in 535 male individuals who were free of vascular disease and in 2249 male subjects who underwent coronary angiography, and analysed the relation of both gene variations to CAD and MI. Both gene **polymorphisms** were in linkage disequilibrium (P<0.0001). Coronary artery disease: the PON54 gene **polymorphism** was not associated with an increased **risk** of CAD. In the total sample and also in younger subjects, an association of the PON191 gene variation with the **risk** of CAD was not detected when the control group of individuals without coronary heart disease was compared with patients with at least one diseased vessel (verified by coronary angiography). In individuals younger than 62 years, a moderate increase in the **relative risk** of CAD associated with the PON191 R allele (1.45 (1. 08-1.95); P=0.015) were found, when subjects without vessel disease (verified by coronary angiography) were compared with CAD patients. Myocardial infarction: an association of the PON54 gene variation with MI was not detected when the control group of individuals without coronary heart disease were compared with patients with at least one MI. A marginal increase in the **risk** of MI associated with the PON54 LL **genotype** (OR 1.27 (1.05-1.51); P=0.011) were detected when patients without MI but with coronary angiography were compared with MI positive patients. Subgroup analyses of low- and high-**risk** populations did not reveal any association of both PON gene **polymorphisms** with CAD or MI. CONCLUSION: The present findings do not strengthen the hypothesis that the paraoxonase gene **polymorphisms** are independently associated with coronary heart disease indicating that these gene variations are of little usefulness as genetic markers of **cardiovascular** disease.

L3 ANSWER 46 OF 57 MEDLINE on STN
Full Text

AN 2000403091 MEDLINE
DN PubMed ID: 10837089
TI Analysis of CYP21 coding **polymorphisms** in three ethnic populations: further evidence of nonamplifying CYP21 alleles among whites.
AU Ozturk I C; Wei W L; Palaniappan L; Rubenfire M; Killeen A A
CS Department of Pathology, University of Michigan Medical School, Ann Arbor, MI 48109, USA.
SO Molecular diagnosis : a journal devoted to the understanding of human disease through the clinical application of molecular biology, (2000 Mar) Vol. 5, No. 1, pp. 47-52.
Journal code: 9614965. ISSN: 1084-8592.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 1 Sep 2000
Last Updated on STN: 1 Sep 2000
Entered Medline: 21 Aug 2000
AB BACKGROUND: Adrenal steroid 21-hydroxylase is essential for the synthesis of both mineralocorticoids and glucocorticoids. The gene for this enzyme, CYP21, contains several frequent coding **polymorphisms**. Because of its essential function in steroid synthesis, **polymorphisms** in this enzyme might influence a variety of disease processes. However, before disease-association studies are performed, it is important to understand the frequency of these **polymorphisms** among normal individuals. METHODS: Using polymerase chain reaction (PCR) with restriction enzyme digestion or size length **polymorphism** analysis, we measured the frequencies of the +Leu(10), Arg102Lys, and Ser268Thr **polymorphisms** in CYP21 in healthy whites, blacks, and Indian Americans. The subjects were all young female college students participating in a study of **relative risks** for **cardiovascular** disease in these populations. RESULTS: The frequency of each **polymorphism** among whites, blacks, and Indian Americans were as follows: +Leu(10), 0.55, 0.96, 0.75; Arg102, 0.63, 0.97, 0.82; and Ser268, 0.92, 0.68, 0.79, respectively. With the exception of the frequencies of the Ser268Thr **polymorphism** among blacks and Indian Americans, there were significantly different frequencies of each **polymorphism** among all groups (P<.05). Among whites, the distribution of **genotypes** for the +Leu(10) and Arg102Lys **polymorphisms** deviated significantly from expected Hardy-Weinberg values because of an excess of homozygotes. CONCLUSIONS: Among the ethnic groups, there are statistically significant differences in the frequencies of these common coding **polymorphisms** in CYP21 that need to be considered in disease-association studies. Deviation from Hardy-Weinberg distributions might be explained by allelic dropout during PCR, a phenomenon previously reported at this locus.

L3 ANSWER 47 OF 57 MEDLINE on STN
Full Text
AN 2000086782 MEDLINE
DN PubMed ID: 10618306
TI Plasminogen activator inhibitor 4G **polymorphism** is associated with decreased **risk** of cerebrovascular mortality in older women.
AU Roest M; van der Schouw Y T; Banga J D; Tempelman M J; de Groot P G; Sixma J J; Grobbee D E
CS Julius Center for Patient Oriented Research, Department of Hematology, Graduate School of Biomembranes, Utrecht University Medical School, Netherlands.. M.Roest@jc.azu.nl
SO Circulation, (Jan 4-11 2000) Vol. 101, No. 1, pp. 67-70.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200002
ED Entered STN: 9 Mar 2000
Last Updated on STN: 9 Mar 2000
Entered Medline: 24 Feb 2000
AB BACKGROUND: A common 4G allele of a 4G/5G **polymorphism** in the promoter region of the plasminogen activator inhibitor-1 (PAI-1) gene is associated with increased transcription of the PAI-1 protein, which may lead to decreased fibrinolysis. It has therefore been proposed as a candidate **risk** factor for myocardial infarction or stroke. METHODS AND RESULTS:

We studied the relationship between PAI-1 4G/5G **genotype** and the **risk** of **cardiovascular** mortality in a prospective cohort study among 12 239 women initially aged between 52 and 67 years, with a maximum follow-up time of 18 years (153 732 follow-up years). PAI-1 4G/5G **genotype** was measured in DNA obtained from urine samples, which were collected at baseline, of 498 women who died of a **cardiovascular** disease and a random sample of 512 women from the same cohort who did not die of **cardiovascular** disease. The PAI-1 4G/5G **genotype** was not associated with **risk** of myocardial infarction or other **cardiovascular** mortality. However, PAI-1 4G4G homozygotes had a markedly reduced **risk** of cerebrovascular mortality compared with PAI-1 5G5G homozygotes: the **relative risk** was 0.4, with a 95% CI of 0.2 to 0.7, whereas the **relative risk** of cerebrovascular mortality in PAI-1 4G5G heterozygotes compared with PAI-1 5G5G homozygotes was 0.7, with a 95% CI of 0.4 to 1.1. CONCLUSIONS: These findings are suggestive of an important contribution of PAI-1 in cerebrovascular pathology, probably via pathways other than fibrinolysis. PAI-1 may protect against destabilization of the atherosclerotic plaque, or it may inhibit neurotoxicity of tissue plasminogen activator in the brain.

L3 ANSWER 48 OF 57 MEDLINE on STN
Full Text
AN 2000051392 MEDLINE
DN PubMed ID: 10582985
TI Association of the platelet glycoprotein IIb HPA-3 **polymorphism** with survival after acute ischemic stroke.
AU Carter A M; Catto A J; Bamford J M; Grant P J
CS Unit of Molecular Vascular Medicine, Research School of Medicine, University of Leeds, Leeds General Infirmary, and Department of Neurology, St. James' University Hospital, Leeds, UK.
SO Stroke; a journal of cerebral circulation, (1999 Dec) Vol. 30, No. 12, pp. 2606-11.
Journal code: 0235266. ISSN: 0039-2499.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 13 Jan 2000
Last Updated on STN: 13 Jan 2000
Entered Medline: 10 Dec 1999
AB BACKGROUND AND PURPOSE: The role of **polymorphisms** of the platelet glycoprotein (GP) IIb/IIIa receptor in the development of **cardiovascular** disease has been the subject of intensive research. The aim of this study was to determine the association of the HPA-3 **polymorphism** of platelet GPIIb with ischemic stroke and subsequent survival and to identify possible interactions of HPA-3 with classic **risk** factors. METHODS: HPA-3 **genotype** was determined by restriction fragment length **polymorphism** in 515 patients with ischemic stroke and 423 healthy, age-matched control subjects. RESULTS: There was no significant difference in the **genotype** distribution of patients and controls, nor was there any difference when patients were subclassified into small- and large-vessel disease. The **genotype** distribution of the 231 patients subsequently dying during 2.8 years of follow-up (aa=45.0%, ab=46.8%, bb=8.2%) was significantly different from that of those still alive (aa=37.0%, ab=48.2%, bb=14. 8%) (P=0.03). In a Cox regression model, the **relative risks** for poststroke mortality in patients of aa and ab **genotype** compared with those of bb **genotype** were 2.42 (95% CI, 1.24 to 4.71) and 2.13 (95% CI, 1.09 to 4.17), respectively, after we accounted for confounding factors. In addition, significant interactions of HPA-3 with the Pl(A) **polymorphism** of GPIIIa (P=0.002) and with fibrinogen (P=0.01) were identified in relation to mortality. CONCLUSIONS: HPA-3 is related to poststroke mortality, and the significant interaction of HPA-3 with Pl(A) and fibrinogen suggests that it may in some way influence the interaction of GPIIb/IIIa with fibrinogen, particularly in the presence of high fibrinogen.

L3 ANSWER 49 OF 57 MEDLINE on STN
Full Text
AN 1999438104 MEDLINE
DN PubMed ID: 10506586

TI **Genotyping** and functional analysis of a polymorphic (CCTTT)(n) repeat of NOS2A in diabetic retinopathy.
AU Warpeha K M; Xu W; Liu L; Charles I G; Patterson C C; Ah-Fat F; Harding S; Hart P M; Chakravarthy U; Hughes A E
CS Department of Medical Genetics, Ophthalmology and Vision Sciences, Queen's University, Belfast, UK.
SO The FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (1999 Oct) Vol. 13, No. 13, pp. 1825-32.
Journal code: 8804484. ISSN: 0892-6638.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199911
ED Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 2 Nov 1999
AB Accumulating evidence shows that the severity and rapidity of onset of diabetic retinopathy are influenced by genetic factors. Expression of the nitric oxide synthases is altered in the retinal vasculature in the early stages of diabetic retinopathy. We analyzed the allele distribution of a polymorphic pentanucleotide repeat within the 5' upstream promoter region of the NOS2A gene in samples of diabetic patients. In diabetic patients from Northern Ireland, the 14-repeat allele of the NOS2A marker was significantly associated with the absence of diabetic retinopathy. Carriers of this repeat had 0.21-fold the **relative risk** of developing diabetic retinopathy than noncarriers of this allele. They also had significantly fewer renal and **cardiovascular** complications. The ability of differing numbers of (CCTTT)(n) pentanucleotide repeats to induce transcription of the NOS2A gene was analyzed using a luciferase reporter gene assay in transfected colonic carcinoma cells. Interleukin 1beta (IL-1beta) induction was most effective in constructs carrying the 14-repeat allele. When cells were incubated in 25 mM glucose to mimic the diabetic state, IL-1beta induction was inhibited in all cases, but to a significantly lesser extent with the 14-repeat allele. These unique properties of the 14-repeat allele may confer selective advantages in diabetic individuals, which may delay or prevent microvascular complications of diabetes.

L3 ANSWER 50 OF 57 MEDLINE on STN
Full Text
AN 1999117312 MEDLINE
DN PubMed ID: 9918518
TI Prospective evaluation of the angiotensin-converting enzyme insertion/deletion **polymorphism** and the **risk** of stroke.
AU Zee R Y; Ridker P M; Stampfer M J; Hennekens C H; Lindpaintner K
CS Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Boston, Mass 02115, USA.. rylz@calvin.bwh.harvard.edu
NC CA-40360 (United States NCI)
K04-HL-03138-01 (United States NHLBI)
R01-HL-56411-01 (United States NHLBI)
+
SO Circulation, (1999 Jan 26) Vol. 99, No. 3, pp. 340-3.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199902
ED Entered STN: 23 Feb 1999
Last Updated on STN: 23 Feb 1999
Entered Medline: 11 Feb 1999
AB BACKGROUND: The D/I **polymorphism** of the ACE gene has been studied in relation to a variety of **cardiovascular** disorders, including stroke. A number of small studies have been conducted, with inconsistent results. We investigated the association between ACE **genotype** and the incidence of stroke in a large, prospective, matched case-control sample from the

Physicians' Health Study. METHODS AND RESULTS: In the Physicians' Health Study, 348 subjects who had been apparently healthy at enrollment suffered a stroke during 12 years of follow-up, as determined from medical records and autopsy. A total of 348 cases were matched by age, time of randomization, and smoking habit to an equal number of controls (who had remained free of stroke). The D/I **polymorphism** was determined by polymerase chain reaction. Data were analyzed for the entire nested case-control sample, and also among a subgroup without a history of hypertension or diabetes mellitus, considered to be at low conventional **risk** (207 cases and 280 controls). All observed **genotype** frequencies were in Hardy-Weinberg equilibrium. The **relative risk** associated with the D allele was 1.11 (95% CI, 0.90 to 1.37; P=0.35), assuming an additive model in the matched analysis. Additional analyses assuming dominant or recessive effects of the D allele, as well as the analysis after stratification for low-**risk** status, showed no material as a statistically significant association. CONCLUSIONS: The results of this large, prospective study indicate that the ACE D/I gene **polymorphism** is not associated with subsequent **risk** of stroke.

L3 ANSWER 51 OF 57 MEDLINE on STN
Full Text
AN 1998147550 MEDLINE
DN PubMed ID: 9488226
TI Alpha-adducin gene **polymorphism** and **cardiovascular** phenotypes in a general population.
AU Castellano M; Barlassina C; Muiesan M L; Beschi M; Cinelli A; Rossi F; Rizzoni D; Cusi D; Agabiti-Rosei E
CS Department of Medical Sciences, University of Brescia, Italy.
SO Journal of hypertension, (1997 Dec) Vol. 15, No. 12 Pt 2, pp. 1707-10. Journal code: 8306882. ISSN: 0263-6352.
CY ENGLAND: United Kingdom
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 10 Apr 1998
Last Updated on STN: 10 Apr 1998
Entered Medline: 2 Apr 1998
AB BACKGROUND: Previous studies have shown that molecular variants of the cytoskeletal protein adducin may be involved in regulation of blood pressure both in genetic rat hypertension and in human essential hypertension. OBJECTIVE: To investigate the relationship of genetic **polymorphism** of alpha-adducin with blood pressure, **cardiovascular** structure, and some biochemical indexes of **cardiovascular risk** in a sample of general population. DESIGN AND METHODS: A sample of 246 subjects (124 men and 122 women, aged 57.7+/-3.7 years) was randomly chosen from a middle-aged population. Twenty-four-hour ambulatory blood pressure, as well as left ventricular mass (by echocardiographic methods) and carotid wall thickness (by B-mode ultrasound methods) were measured. DNA was extracted from peripheral blood samples; the Gly460Trp diallelic variant of human alpha-adducin was **genotyped** by polymerase chain reaction amplification and then allele-specific oligo hybridization. RESULTS: A trend toward higher 24 h ambulatory blood pressure values in subjects not treated with antihypertensive drugs was observed among carriers of Trp460 allele, although the differences did not attain statistical significance (at closest, P = 0.066 for a dominant effect of Trp460 on systolic blood pressure). When blood pressure was considered a dichotomous variable, allowing the inclusion of treated hypertensives), a higher prevalence of Trp460 allele among hypertensives was observed (0.188 versus 0.106 among normotensives, P= 0.02). There was no evidence of association either of left ventricular mass or of common carotid wall thickness with Gly460Trp **polymorphism**. CONCLUSIONS: In this sample of a general population, the relationship of a genetic **polymorphism** of alpha-adducin with blood pressure values was rather weak. However, a population-based case-control analysis indicated that there was an association between Trp460 allele and hypertension, with a **relative risk** for subjects carrying at least one Trp460 allele of approximately 1.6. Further investigation of larger and different population samples in order to assess the role of adducin gene **polymorphism** as a marker of genetic predisposition to the development of hypertension is warranted.

L3 ANSWER 52 OF 57 MEDLINE on STN
Full Text
AN 1998104012 MEDLINE
DN PubMed ID: 9443775
TI **Polymorphism** of angiotensin converting enzyme, angiotensinogen, and apolipoprotein E genes in a Japanese population with cerebrovascular disease.
AU Nakata Y; Katsuya T; Rakugi H; Takami S; Sato N; Kamide K; Ohishi M; Miki T; Higaki J; Ogihara T
CS Department of Geriatric Medicine, Osaka University Medical School, Suita, Japan.
SO American journal of hypertension : journal of the American Society of Hypertension, (1997 Dec) Vol. 10, No. 12 Pt 1, pp. 1391-5.
Journal code: 8803676. ISSN: 0895-7061.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
ED Entered STN: 26 Feb 1998
Last Updated on STN: 26 Feb 1998
Entered Medline: 19 Feb 1998
AB The homozygous deletion allele of the angiotensin converting enzyme gene (ACE/DD), homozygous threonine allele of the angiotensinogen gene (AGN/TT), and the epsilon4 allele of the apolipoprotein E gene (apoE/epsilon4) are reported to be associated with ischemic heart disease. Cerebrovascular disease (**CVD**) is another atherosclerotic disease; and the effects of these **polymorphisms** on **CVD** have been confusing. In this study, we investigated whether ACE/DD, AGN/TT, and apoE/epsilon4 **genotypes** are associated with **CVD** and whether genetic **risk** is enhanced by the effect of one upon another. We ascertained these **genotypes** in patients with cerebral infarction (n = 55) and cerebral hemorrhage (n = 38), diagnosed by brain computed tomography. Control subjects for the infarction group and the hemorrhage group were randomly selected from 583 subjects matched for age, gender, and history of hypertension with patients. Frequency of ACE/DD **genotype** was higher in the patients with infarction than in the controls (chi2 = 6.1, P < .05). The AGN/TT **genotype** was not associated with either infarction or hemorrhage, but it increased the **relative risk** for cerebral infarction in the subjects with ACE/DD **genotype** (chi2 = 8.0, P < .01, odds ratio; 11.7, 95% confidence intervals: 1.4 to 96.0). There was no significant association between apoE/epsilon4 and **CVD**. These results suggest that ACE/DD predicts cerebral infarction, but not cerebral hemorrhage, and that AGN/TT enhances the **risk** for cerebral infarction associated with ACE/DD.

L3 ANSWER 53 OF 57 MEDLINE on STN
Full Text
AN 1997468699 MEDLINE
DN PubMed ID: 9327764
TI Alu-repeat **polymorphism** in the gene coding for tissue-type plasminogen activator (t-PA) and **risks** of myocardial infarction among middle-aged men.
AU Ridker P M; Baker M T; Hennekens C H; Stampfer M J; Vaughan D E
CS Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA.. pmridker@bics.bwh.harvard.edu
SO Arteriosclerosis, thrombosis, and vascular biology, (1997 Sep) Vol. 17, No. 9, pp. 1687-90.
Journal code: 9505803. ISSN: 1079-5642.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
ED Entered STN: 24 Dec 1997
Last Updated on STN: 29 Jan 1999
Entered Medline: 13 Nov 1997
AB An Alu-repeat **polymorphism** in the gene coding for tissue-type plasminogen activator has been described recently, and it has been hypothesized that this **polymorphism** may predict **risk** of coronary thrombosis. In a prospective cohort of nearly 15,000 apparently healthy men, presence of an Alu-repeat insertion/deletion (I/D) **polymorphism** in the gene coding for tissue-type plasminogen activator was determined among

369 study participants who subsequently suffered a first myocardial infarction (cases) and among a group of 369 age- and smoking-matched study participants who remained free of reported **cardiovascular** disease during follow-up (controls). The distributions of the II, DI, and DD **genotypes** of the tissue-type plasminogen activator **polymorphism** among men who subsequently suffered myocardial infarction (0.30, 0.50, 0.21) were virtually identical to those who remained free of disease (0.29, 0.50, 0.21; P = .9). There was no evidence of association between the Alu insertion **polymorphism** and **risks** of future myocardial infarction in models assuming either allelic recessive (**relative risk**, 1.05; 95% confidence interval, 0.8 to 1.4, P = .8) or allelic dominant (**relative risk**, 1.04; 95% confidence interval, 0.7 to 1.5, P = .8) modes of inheritance, nor were associations found in analyses stratified by age, family history, hypercholesterolemia, or the presence of other **risk** factors for premature coronary disease. Multivariate analysis had no important effects on these relationships. In this cohort of middle-aged US men, the presence of the insertion allele of the Alu-repeat **polymorphism** of the tissue-type plasminogen activator gene is not associated with future **risks** of myocardial infarction.

L3 ANSWER 54 OF 57 MEDLINE on STN
Full Text
AN 1997336683 MEDLINE
DN PubMed ID: 9193430
TI Tissue plasminogen activator and **risk** of myocardial infarction. The Rotterdam Study.
AU van der Bom J G; de Knijff P; Haverkate F; Bots M L; Meijer P; de Jong P T; Hofman A; Kluft C; Grobbee D E
CS Department of Epidemiology and Biostatistics, Erasmus University Medical School, Rotterdam, Netherlands.
SO Circulation, (1997 Jun 17) Vol. 95, No. 12, pp. 2623-7.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199707
ED Entered STN: 24 Jul 1997
Last Updated on STN: 29 Jan 1999
Entered Medline: 17 Jul 1997
AB BACKGROUND: Impaired fibrinolytic capacity, as assessed by euglobulin clot lysis time or plasma concentration of fibrinolytic parameters, has been associated with an increased **risk** of myocardial infarction (MI). We studied the association of a **polymorphism** in the gene for TPA and of plasma concentrations of TPA (antigen and activity) with the prevalence of MI. METHODS AND RESULTS: A case-control study was performed. Subjects with a history of MI (n = 121) and controls (n = 250) were drawn from the Rotterdam Study, a population-based cohort study of 7983 subjects > or = 55 years old. We determined TPA antigen and activity in plasma and **genotyped** all subjects for the Alu repeat insertion/deletion **polymorphism** in intron h in the TPA gene. Homozygosity for the insertion was associated with twice as many cases of MI as was homozygosity for the deletion (odds ratio, 2.24; 95% CI, 1.11-4.50). TPA antigen was positively associated with the **risk** of MI; compared with that in the lowest quartile, the **relative risks** (odds ratio) in the second, third, and upper quartiles were 1.7 (CI, 0.9-3.3), 2.3 (1.2-4.4), and 2.0 (1.0-3.8), respectively. When adjusted for body mass index, HDL and total cholesterol, systolic and diastolic blood pressures, and current smoking, the **risk** associated with TPA antigen concentration was attenuated. Increased concentrations of TPA activity tended to be associated with an increased **risk** of MI. CONCLUSIONS: This study provides evidence for an independent association of the insertion allele of the insertion/deletion **polymorphism** in the TPA gene with nonfatal MI. Increased TPA antigen is associated with an increased **risk** of MI; however, this association was not independent of **cardiovascular** disease **risk** factors.

L3 ANSWER 55 OF 57 MEDLINE on STN
Full Text
AN 1997027514 MEDLINE
DN PubMed ID: 8873653

TI Genetic **polymorphism** of methylenetetrahydrofolate reductase and myocardial infarction. A case-control study.
AU Schmitz C; Lindpaintner K; Verhoef P; Gaziano J M; Buring J
CS Division of Cardiovascular Diseases, Brigham and Women's Hospital, Boston, MA 02115, USA.
NC K04-HL-03138-01 (United States NHLBI)
SO Circulation, (1996 Oct 15) Vol. 94, No. 8, pp. 1812-4.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199612
ED Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
Entered Medline: 16 Dec 1996
AB BACKGROUND: Elevated total plasma homocyst(e)ine (tHcy; the composite of homocysteine-derived moieties in their oxidized and reduced forms) levels are a **risk** factor for coronary heart disease, stroke, and venous thrombosis. tHcy plasma levels are influenced by folate, vitamins B6 and B12, as well as by hereditary factors. A point mutation (C677T) in the gene encoding methylenetetrahydrofolate reductase, an enzyme involved in homocysteine remethylation, has been reported to render the enzyme thermolabile and less active and has been associated with elevated tHcy in homozygous carriers (+/+ **genotype**) as well as with increased **risk** of premature **cardiovascular** disease. METHODS AND RESULTS: We investigated whether this mutation influences **risk** for myocardial infarction (MI) and plasma levels of tHcy and whether this effect may be modified by dietary folate intake in 190 MI cases and 188 control subjects from the Boston Area Health Study. **Genotype** frequencies were 37.8% for -/-, 47.8% for +/-, and 14.4% for +/+ in the control group and 50.0% for -/-, 34.7% for +/-, and 15.3% for +/+ in the case group. The **relative risk** for MI associated with the +/+ **genotype** (compared with +/- and -/-) was 1.1 (95% CI, 0.6 to 1.9; P = .8). Stratification by folate intake values above and below the median did not significantly alter these results. Plasma tHcy levels were 9.9 +/- 2.7 mumol/L in -/- individuals, 10.6 +/- 3.8 mumol/L in +/- individuals, and 9.1 +/- 2.3 mumol/L in +/+ individuals (Ptrend = NS; determined in 68 cases and 59 control subjects). CONCLUSIONS: Our data show that homozygosity for the C677T mutation in this largely white, middle-class US population is not associated with increased **risk** for MI, irrespective of folate intake. This suggests that this mutation does not represent a useful marker for increased **cardiovascular risk** in this and in similar populations.

L3 ANSWER 56 OF 57 MEDLINE on STN
Full Text
AN 1996177833 MEDLINE
DN PubMed ID: 8598840
TI Absence of association or genetic linkage between the angiotensin-converting-enzyme gene and left ventricular mass.
AU Lindpaintner K; Lee M; Larson M G; Rao V S; Pfeffer M A; Ordovas J M; Schaefer E J; Wilson A F; Wilson P W; Vasan R S; Myers R H; Levy D
CS Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA.
NC K04-HL03138-01 (United States NHLBI)
N01-38038
RR03655 (United States NCRR)
SO The New England journal of medicine, (1996 Apr 18) Vol. 334, No. 16, pp. 1023-8.
Journal code: 0255562. ISSN: 0028-4793.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199604
ED Entered STN: 6 May 1996
Last Updated on STN: 6 Feb 1998
Entered Medline: 25 Apr 1996
AB BACKGROUND. Homozygous carries of the D allele of the

angiotensin-converting-enzyme (ACE) gene have been reported to be at increased **risk** for various **cardiovascular** disorders, including left ventricular hypertrophy. We investigated the potential role of the ACE gene in influencing left ventricular mass. METHODS. Quantitative echocardiographic data and DNA samples were available for 2439 subjects from the Framingham Heart Study. ACE **genotypes** were determined by an assay based on the polymerase chain reaction. (The D allele of the ACE gene contains a deletion, whereas the I [insertion] allele does not.) Left ventricular mass and the prevalence of left ventricular hypertrophy, adjusted for clinical covariates, were analyzed according to **genotype**. Genetic linkage between the ACE locus and left ventricular mass was evaluated by quantitative analysis of pairs of siblings. RESULTS. The ACE **genotype** was associated neither with left ventricular mass nor with the prevalence of left ventricular hypertrophy. Mean (+/-SE) left ventricular mass (adjusted for sex) among subjects carrying the DD, DI, and II **genotypes** was 165+/-1.6, 165+/-1.3, and 166+/-2.0 g, respectively (P=0.90). The prevalence of left ventricular hypertrophy among the three **genotype** groups was 15.6 percent, 13.6 percent, and 15.6 percent, respectively (P=0.36), and the adjusted **relative risk** of left ventricular hypertrophy associated with the DD **genotype** was 1.10 (95 percent confidence interval, 0.86 to 1.19). Linkage analysis in 759 pairs of siblings using both the ACE D/I marker and a microsatellite **polymorphism** at the neighboring locus for the human growth hormone gene failed to support any role of ACE in influencing left ventricular mass. CONCLUSIONS. The ACE **genotype** showed no association with echocardiographically determined left ventricular mass, nor did it confer an increased **risk** of left ventricular hypertrophy. We found no appreciable role of the ACE gene in influencing left ventricular mass.

L3 ANSWER 57 OF 57 MEDLINE on STN
Full Text
AN 1994224801 MEDLINE
DN PubMed ID: 8170965
TI Insertion/deletion **polymorphism** of the angiotensin-converting enzyme gene is strongly associated with coronary heart disease in non-insulin-dependent diabetes mellitus.
AU Ruiz J; Blanche H; Cohen N; Velho G; Cambien F; Cohen D; Passa P; Froguel P
CS Centre d'Etude du Polymorphisme Humain, (Fondation Jean Dausset-CEPH), Paris, France.
SO Proceedings of the National Academy of Sciences of the United States of America, (1994 Apr 26) Vol. 91, No. 9, pp. 3662-5.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 13 Jun 1994
Last Updated on STN: 13 Jun 1994
Entered Medline: 1 Jun 1994
AB Non-insulin-dependent diabetes mellitus (NIDDM) is considered a model of premature atherosclerosis with a strong genetic component. We have investigated the role of angiotensin-converting enzyme (ACE; EC 3.4.15.1) gene in 316 unrelated NIDDM individuals, 132 who had myocardial infarction or significant coronary stenoses and 184 with no history of coronary heart disease (CHD). A deletion-**polymorphism** in the ACE gene was recently reported to be associated with myocardial infarction especially in people classified as low **risk**. Here we report that the D allele of the ACE gene is a strong and independent **risk** factor for CHD in NIDDM patients. The D allele is associated with early-onset CHD in NIDDM, independently of hypertension and lipid values. A progressively increasing **relative risk** in individuals heterozygous and homozygous for the D allele was observed (odds ratios of 1.41 and 2.35, respectively; P < 0.007), suggesting a codominant effect on the **cardiovascular risk**. The percentage of CHD attributable to the ACE deletion allele was 24% in this NIDDM population. Identification of NIDDM patients carrying this putative CHD-susceptibility **genotype** would help early detection and treatment of CHD.

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=> s baysnp
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L4           0 BAYSNP

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     FILE 'MEDLINE' ENTERED AT 12:35:58 ON 22 OCT 2008
L1          2144 S GENOTYP? AND RISK AND (CARDIOVASCULAR OR (CARDIO AND VASCULAR
L2            80 S L1 AND RELATIVE RISK
L3            57 S L2 AND (SNP OR POLYMORPHISM)
L4             0 S BAYSNP

=> log y
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
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FULL ESTIMATED COST                                 34.43      34.64

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